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LIENO-PORTAL VENOGRAPHY IN THE STUDY OF PORTAL CIRCULATION IN THE DOG

by

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A filling of collaterals, a retarded flow of contrast medium, and widening of the splenic and portal veins in lieno-portal venography are regarded as signs of portal obstruction. The purpose of the present investigation was to check whether factors other than portal obstruction might also be capable of producing these roentgenographic changes.

Earlier investigations in dogs

In an investigation of the possibilities of lieno-portal venography ABEATICI and CAMPI (1951 and 1952) obtained no filling of collaterals in normal animals. They ligated the splenic vein in an attempt to produce splenomegaly. In none of the animals did this measure produce the desired effect, but within 1 to 20 days collaterals were regularly demonstrated in the lieno-portal venogram.

In small materials BAHNSON et coll. (1953) and DAVIS et coll. (1955) obtained a filling of collaterals after ligation of the splenic vein or the portal vein but never otherwise.

DREYER (1954) demonstrated collaterals in 4 animals in which the portal vein had been ligated. No such filling was obtained in any of 7 controls. On the basis of these findings he claimed that roentgenographic demonstration of collaterals suggests portal obstruction with reversed direction of flow of the blood in these vessels. He found neither the injection of the contrast medium nor rapid injection of 20 ml saline into the spleen to have any demonstrable effect on the portal pressure in any of the 6 experimental animals. With the aid of an automatic film changer

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DREYER showed that contrast medium injected into the spleen reached the hilum of the liver within 1 second of the beginning of the injection.

In another paper based on lieno-portal venograms of 15 patients and 9 dogs DREYER (1954) discussed 'streamlining' in the portal vein. He obtained an equally good filling of the portal branches of the right and left lobes of the liver.

LEROUX and DE SCOVILLE (1954) obtained no filling of collaterals in 6 dogs (10 examinations). Using serial roentgenography they found the contrast medium to require 0.6 to 3 seconds to pass from the spleen to the bifurcation of the portal vein. They ascribed this variation in the velocity of the contrast medium to differences in the rate of injection (0.6 to 1.1 ml/sec).

Thus judging from the literature, a filling of collaterals is obtained only if the portal vein or the splenic vein is occluded.

Material and methods

The material consisted of 19 dogs. Of these, 17 weighed 8 to 14 kg and 2 about 20 kg.

The animals were deprived of food for 12 hours before the examination which was carried out under anesthesia (Nembutal, Abbot, 30 mg/kg body weight) and endotracheal intubation. Following laparotomy a portal tributary was catheterised and the pressure registered with a saline manometer (zero-line: right auricle). The pressure in the inferior vena cava was measured with a catheter passed via the right femoral vein.

For the routine venographic examination the dogs were placed in the supine position. A dose of 4 to 5 ml of Triurol 50 % (sodium acetrizoate: specific gravity 1.3; viscosity at 37° C 2.1 centipoise) was injected manually in 2 to 3 seconds into the spleen. In order to study any influence of variations in the injection pressure on the lieno-portal venogram, some examinations were carried out with a lower or higher rate of injection of contrast medium. The injection time was measured with a stop-watch. In one dog the investigation was repeated in a prone position. In 6 examinations the contrast medium was injected directly into the splenic vein.

Two thirds of the examinations were carried out with an automatic film changer (up to 6 exposures per second). Only in these examinations was the velocity of flow of the contrast medium assessed. (Technical data: F. F. D. 90 to 100 cm; 70 to 90 kV; 300 to 500 mA; 0.023 to 0.10 sec.)

All vessels branching from the splenic vein or the portal vein were regarded as collaterals, even if they were only filled in 0.5 cm of their length. The width of the column of contrast medium in the splenic vein just before it enters the portal vein was taken as the width of the splenic vein. Layer formation between the contrast medium and the blood from the superior mesenteric vein often made it difficult to judge the width of the portal vein.

The velocity of flow was measured as follows:

1) The rate of flow of the tip of the column of contrast medium in cm/sec, as judged by the greatest distance between any 2 consecutive exposures.

2) The interval between the moment the injection of the contrast medium was started and the moment the contrast medium reached the bifurcation of the portal vein (spleen-hilum time).

Up to ten examinations were carried out on each dog within 2 to 6 hours without any obvious deterioration in the general condition of the animal. Neither had these repeated injections of 4 to 8 ml of contrast medium any demonstrable effect on the portal pressure, the appearance of the collaterals, the width of the vessels, or velocity of the flow.

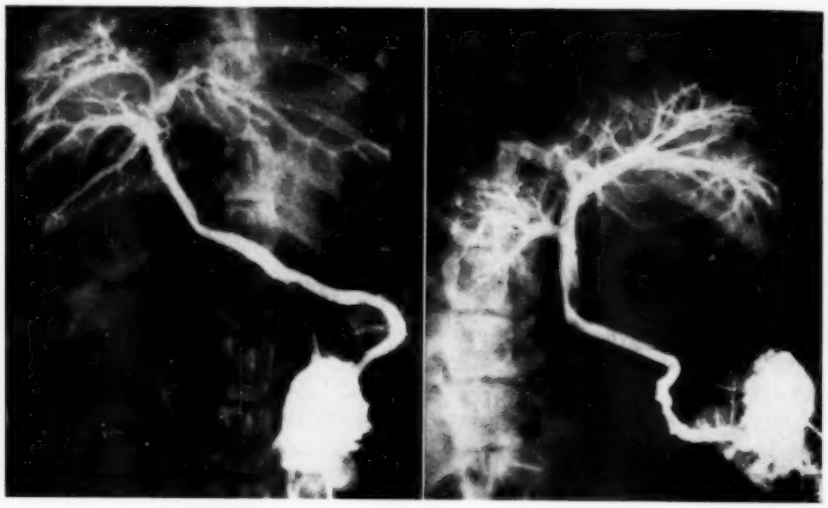
Lieno-portal venography in normal dogs

The pressure in the portal vein varied between 9 and 14 cm H_2O in 16 dogs examined. In routine lieno-portal venographic examinations the contrast medium filled the splenic vein and the major portion of the lumen of the portal vein with its intrahepatic branches. Layer formation often occurred in the portal vein on entry of the contrast mixture from the splenic vein and of the blood from the mesenteric veins. When the animals were examined in the supine position (Fig. 1 a), the vessels in the left part of the liver became demonstrable later and less distinctly than those in the right. One of the animals examined in the supine position was afterwards examined prone, though it was turned somewhat to the left. In this position a better filling was obtained of the vessels in the left part of the liver than in the right (Fig. 1 b). On slow injection (down to 1 ml in 8 sec) signs of layer formation between the contrast mixture and the blood occurred even in the splenic vein. With this slow rate of injection the column of contrast medium was narrower and no filling was obtained of the veins running in a ventral direction owing to the relatively heavier contrast medium flowing along the floor of the vessel.

A filling of collaterals was obtained in 5 of 17 dogs (routine examinations failed in 2). No difference was found between the portal pressure in dogs with and without demonstrable collaterals. In 16 animals (1 failure) the width of the splenic vein ranged between 5 and 7 mm. No difference in width of the splenic vein was found between the animals

Table 1

Case	Occurrence of collaterals	Spleen-hilum time (seconds)	Velocity of flow (cm/sec)
D	—	1	22
E	—	1	22—24
G	—	1	21
H	—	1	21
M	—	1—2	> 11
N	—	1—2	> 11
L	+	3	11
P	+	2	8—12
R	+	2—3	10—11
S	+	3—4	8—10



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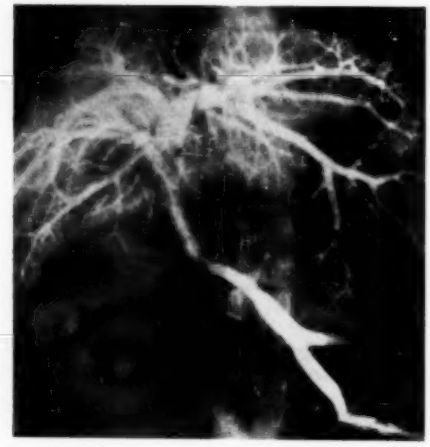

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Fig. 1. Normal dog. a) Lieno-portal venogram. Supine. b) Lieno-portal venogram. Prone. c) Portal venogram after injection of contrast medium directly into the splenic vein.

with and without demonstrable collaterals. In the presence of demonstrable collaterals the velocity of flow was lower (Table 1). Histologic examination of the liver of 3 of the dogs in which collaterals had been demonstrated showed no signs of a pathologic condition.

Within 0.5 to 1 minute of every injection of contrast medium a rapid transient increase of 2 to 4 cm H_2O in portal pressure was noted. Three examinations were carried out during this increased pressure. In these venograms a filling was obtained of fewer intrahepatic branches than in venograms taken in exactly the same way but just before the increase in pressure. Injection of saline did not produce any such increase in pressure.

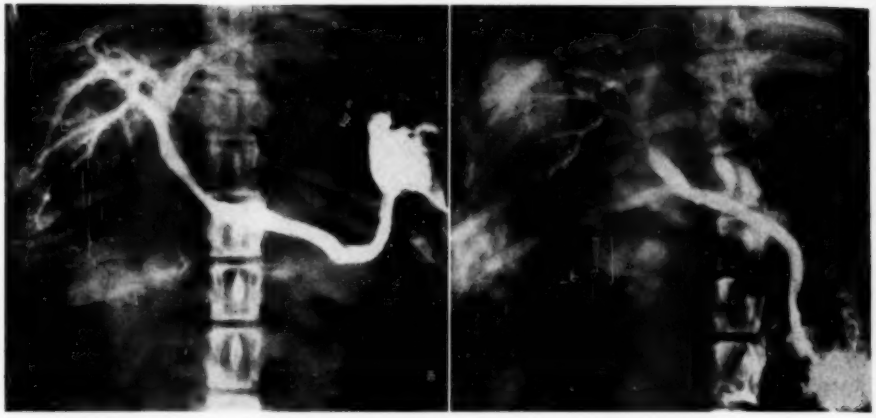
Influence of site and rate of injection of contrast medium on venogram. Injection of contrast medium into the spleen was never attended by any increase in the portal pressure, not even when 8 ml of contrast medium was injected within 1 sec. Neither did rapid injection of 20 ml saline produce any change in the portal pressure during injection.

Two animals in which collaterals had not been demonstrable on examination by the routine technique were afterwards re-examined (one 3 times) with an injection of up to 8 ml contrast medium per second. Even then no collaterals were demonstrable. Neither were any changes noted in the width of the vessels. The velocity of flow of the contrast medium was not higher, but, if anything, lower, and the pool of contrast medium around the tip of the needle in the spleen was larger. No contraction of the spleen was noted.

Two dogs in which collaterals were demonstrated on examination by the routine technique were re-examined twice with a much lower rate of injection and a smaller dose of contrast medium (down to 1 ml per 8 seconds). In 3 of the 4 examinations the collaterals were still demonstrated. In the fourth, in which no filling was obtained of any collaterals, the filling of the intra-hepatic portal vessels was also incomplete. The velocity of flow recorded was the same as that found on injection by the routine technique but the column of contrast medium in the splenic vein was narrower owing to layer formation.

In 3 dogs examined after ligation of all arteries to the spleen the contrast medium passed from the splenic parenchyma to the splenic vein at the same rate as in normal dogs (less than 1 sec). Ligation of the splenic artery produced no change in the velocity of flow (spleen-hilum time 1 to 1.5 sec), but a narrowing of the splenic vein.

Three dogs, in which the lieno-portal venogram by the routine technique showed no collaterals, were afterwards examined with *injection of contrast medium directly into the splenic vein* at the same rate (Fig.1 c). During this injection the portal pressure increased 1 to 3 cm and collaterals were demonstrahle. The width of the vessels on injection of contrast medium into the splenic vein persisted unchanged in 1 and increased in 2. In the animal in which the velocity of flow could be evaluated it was much higher on injection into the splenic vein than on injection into the spleen (spleen-hilum time: 0.3 and 1 sec respectively).



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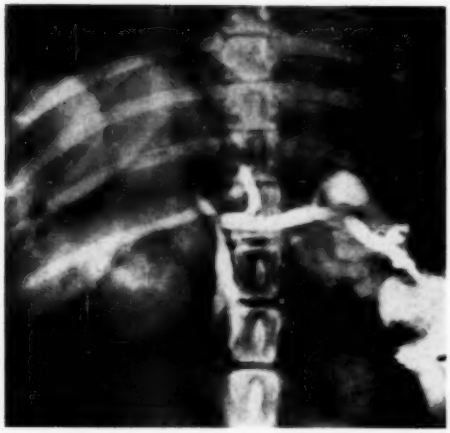

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Fig. 2. Lieno-portal venogram in experimental pre-hepatic stasis. a) before, b) after partial, and c) after total portal ligation in one and the same dog.

Lieno-portal venography in dogs with increased portal pressure.

Prehepatic stasis. Thirty examinations were carried out in 7 dogs without and with a varying degree of portal occlusion. This was produced by placing a course linen ligature around the portal vein, the desired degree of occlusion being secured by varying the tightness of the ligature. Lieno-portal venograms were obtained before and up to 60 minutes after ligation of the portal vein (Fig. 2).

On total portal ligation the portal pressure increased by 8 to 53 cm H_2O (mean 29 cm H_2O) in 7 dogs. In 3 the portal vein was ligated for 30 to 60 minutes and in these the portal pressure decreased from 54 to 28, 33 to 16, and 65 to 49 cm H_2O, respectively. In 2 animals collaterals appeared even before portal ligation and were wider and demonstrable further out in the periphery after the ligature had been drawn tight. This widening and increased filling was still more pronounced after portal ligation for 30 to 60 minutes.

On slight tightening of the portal ligature the portal pressure increased by 7 to 13 cm H_2O in 3 animals. Even this small increase in the portal pressure resulted in a filling of collaterals.

On complete ligation of the portal vein the column of contrast medium did not reach the ligature in 6 of 7 examinations (Fig. 2 c). On slight occlusion, on the other hand, the portal vein was filled in all of the animals studied. On occlusion of the portal vein a slight widening of the splenic vein was noted in 5 of the 7 animals examined. The velocity of flow was determined in only 3 animals. In these it decreased from 22 to 16, 11 to 6, and 10 to 4—8 cm/sec, respectively.

Post-hepatic stasis. Eighteen lieno-portal venographic examinations were carried out on 6 dogs before and after post-hepatic stasis

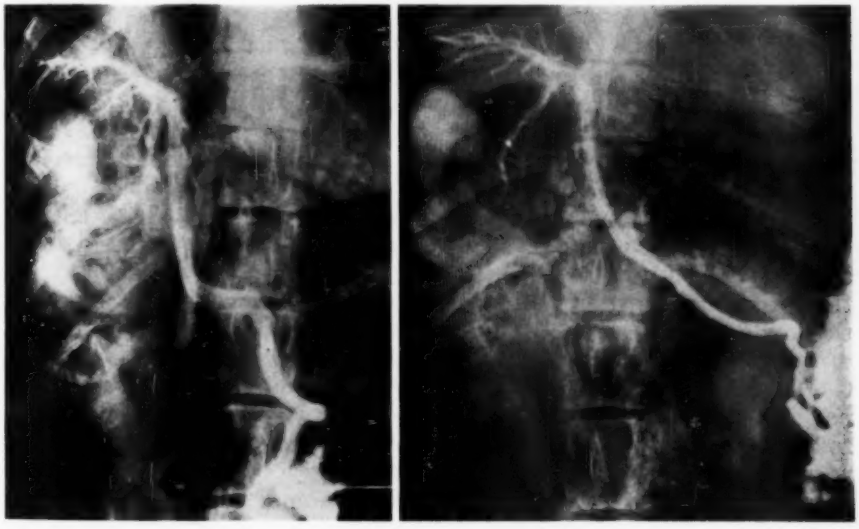

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Fig. 3. Lieno-portal venogram in artificially increased intra-abdominal pressure. a) without and b) with increased intra-abdominal pressure in one and the same dog.

produced by insufflation of the lungs with air via a tightly-fitting tracheal tube. The pressure in the portal system and in the inferior vena cava were normally 9 to 10 and 2 to 5 cm H_2O, respectively. Variations in the increase in pressure between 2 to 14 cm H_2O in the portal vein and 3 to 12 cm H_2O in the vena cava were achieved by varying the degree of insufflation of the lungs.

In 4 of the animals without originally demonstrable collaterals, collaterals appeared in 3 when the portal pressure was increased by 2 to 5 cm H_2O. In the fourth animal an increase by as much as 5 cm H_2O failed to produce a filling of the collaterals.

Increased width of the vessels and decreased velocity of flow were common in the presence of post-hepatic stasis.

Increased intra-abdominal pressure. In 3 dogs the intra-abdominal pressure was increased by filling the abdominal cavity with saline. The increase in this pressure thereby produced was attended by a simultaneous increase in the portal pressure and in the pressure in the inferior vena cava. On increase in the portal pressure (12, 21 and 27 cm H_2O, respectively) the vessels regularly became narrower (Fig. 3).

Discussion

In clinical lieno-portal venography with the patient in the supine position the right part of the liver is demonstrated both earlier and better than the left suggesting that the bulk of the splenic blood flows into the right lobe. This is not compatible with what SÉRÉGÉ (1901) and COPHER and DICK (1928) found on injection of dyes into the portal system. They claimed that the splenic blood passes mainly to the left part of the liver and the mesenteric blood to the right part — 'streamlining'. Since the appearance of a normal lieno-portal venogram might be influenced by the higher specific gravity of the contrast medium, views were obtained of the dog both in the supine and prone positions. The declival parts of the liver — the right in the supine position and the left in the prone position — appeared first and best. This suggests that owing to the high specific gravity of the contrast medium lieno-portal venography is unsuitable for the evaluation of 'streamlining'.

We were not able to confirm the observation of LEROUX and DE SCOVILLE (1954) that the velocity of flow is influenced by the rate of injection of contrast medium into the spleen. Furthermore, in the present investigation the portal circulation was not found to be influenced in any respect by the injection of contrast medium into the spleen. Varia-

tion in the rate of injection of contrast medium into this organ in one and the same dog had no influence on the appearance of the collaterals. Neither the portal pressure, the velocity of flow, nor the width of the splenic vein varied with the injection pressure. On the other hand, injection of contrast medium into a portal tributary could produce an increase in the portal pressure with a contrast filling of the collaterals, increased velocity of flow, and increase in the width of the vessels. Contrary to what might be deduced from results on record (Du Boulay and Green 1954), injection into a portal tributary is therefore not suitable for studies of the circulation in the portal system.

The difference between these two methods suggests that the spleen behaves as a cushion absorbing changes in portal pressure on injection of contrast medium. In dogs as in man contrast medium appeared in the splenic vein immediately after the beginning of the injection. Ligation of the splenic artery produced no changes in the lieno-portal venograms.

The above-mentioned findings thus show that in the presence of portal hypertension in human beings a filling of the collaterals might be regarded as a manifestation of reversed flow of blood in these vessels. This type of filling was obtained in all the dogs in which the portal pressure was increased by ligation of the portal vein. This supports the assumption that demonstrable collaterals are a sign of portal obstruction. On such ligation the velocity of flow was also slower and the vessels wider, as in the presence of portal hypertension in man.

It has often been claimed that lieno-portal venography will show whether any obstruction is intrahepatic or extrahepatic (Dreyer 1954; Gvozdanović and Hauptmann 1954, 1955; Lebon et coll. 1954; Atkinson et coll. 1955; Bergstrand and Ekman 1955; Figley et coll. 1955). In a recent clinical series, however, we observed 3 cases of liver cirrhosis with portal hypertension in which no filling was obtained of the splenic vein or of the portal vein despite the absence of any demonstrable thrombosis: contrast medium passed from the splenic hilum via wide collaterals to the caval system. This observation of absence of contrast medium along a patent portion of the vessel before the site of occlusion was also made in experiments in dogs. On complete occlusion of the portal vein no filling was obtained in that section of the vessel nearest the ligature. On partial occlusion, during which a certain passage was possible, the entire portal vein was filled. These observations show that the site of a complete obstruction is not always indicated by the tip of the column of contrast medium.

In man with portal hypertension the increase in the width of the splenic vein and the portal vein was found to be less accentuated in the presence of ascites (Bergstrand and Ekman 1957). This difference might be explained by the observation on dogs that the rise in the intra-abdominal

pressure following infusion of saline produces a diminution of the width of the vessels.

Of 17 normal dogs, collaterals were demonstrable in 5. No such filling was obtained in the absence of portal hypertension in a human series (BERGSTRAND and EKMAN 1957). In dogs in which collaterals were not originally demonstrable, these appeared even on such a small increase in the portal pressure as 2 to 5 cm H_2O.

The observation that the increase in portal pressure in the dog decreases within one hour of total occlusion of the portal vein confirmed OLERUD's (1953) findings. This together with the other findings described above indicates that the collateral circulation in the dog is better developed than in man. This can explain the observation of MORRIS and MILLER (1951) that in dogs it is difficult to produce signs resembling those seen in chronic portal hypertension in man.

Conclusions

Variations in the rate of injection of contrast medium into the spleen in lieno-portal venograms in dogs produced no differences in the portal pressure or film appearances as judged by the absence or presence of collaterals, width of the splenic vein, or the velocity of flow of contrast medium. Injection of the medium directly into the splenic vein, however, was followed by changes in the hemodynamics of the portal system.

Ligation of the splenic artery produced no changes in the appearances noted.

Owing to the relatively high specific gravity of the contrast medium, its distribution in the intrahepatic portal branches varied with the posture of the animal.

Complete ligation of the portal vein produced an increase in portal pressure of 8 to 53 cm H_2O (mean 29 cm H_2O). After complete ligation for 30 to 60 minutes the increase diminished.

As a rule no filling was obtained of the portion of the portal vein nearest to the site of complete obstruction.

In portal stasis collaterals were regularly demonstrable. The vessels were increased in width and the velocity of flow was decreased.

In the presence of increased intra-abdominal pressure the splenic vein was decreased in width.

From these observations it was concluded:

that any increase in pressure on injection of the contrast medium is absorbed by the spleen and thereby not transmitted to the portal circulation;

that lieno-portal venography is therefore a reliable method for judging

the direction of flow of the portal blood, the velocity of portal flow, and the width of the splenic vein, but the method is not acceptable for demonstrating 'streamlining' and the distribution of the portal blood in the liver;

that the changes demonstrated in portal obstruction are due entirely to a pathologic circulation;

that the examination will not always show the site of a portal obstruction;

that in portal obstruction the portal blood is drained by collaterals;

that an increased intra-abdominal pressure — as in ascites — is capable of decreasing the width of the splenic vein, probably because of mechanical pressure.

SUMMARY

An investigation of lieno-portal venography in the study of portal circulation was carried out in 19 dogs to assess the value of the method both in normal conditions and in the presence of portal obstruction. The procedure was found to be a reliable one for determining the direction of flow of the portal blood, the velocity of portal flow, and the width of splenic vein. Certain limitations of the method are discussed.

ZUSAMMENFASSUNG

Eine Untersuchung der lieno-portalen Venographie beim Studium der Portazirkulation wurde an 19 Hunden ausgeführt, um den Wert der Methode unter normalen Bedingungen und bei Anwesenheit einer Portaobstruktion zu bestimmen. Man fand, dass die Methode für die Bestimmung der Flussrichtung und der Strömungsgeschwindigkeit des Portablutes und der Weite der Milzvene zuverlässig ist. Gewisse Begrenzungen der Methode werden besprochen.

RÉSUMÉ

En étudiant la circulation portale les auteurs ont fait un examen de la splénoportographie sur 19 chiens pour déterminer expérimentalement la valeur de cette méthode dans des conditions normales et en présence d'une obstruction portale. Cette expérimentation a prouvé qu'on peut se fier à cette technique pour déterminer le sens de l'écoulement du sang portal, la vitesse de la circulation portale et la largeur de la veine splénique. Les auteurs examinent certaines limites de cette méthode.

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PERCUTANEOUS LIENO-PORTAL VENOGRAPHY

Technique and complications

by

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Organic water soluble contrast media may be injected into the portal system without involving any undue risk in a concentration high enough to demonstrate its anatomy and thereby the vascular pattern of the liver. The contrast media have been injected in different ways:

1. Directly into a portal tributary at laparotomy — portal venography (BLAKEMORE & LORD 1945; DE SOUSA PEREIRA 1949; MOORE & BRIDENBAUGH 1950).

2. Into the splenic parenchyma after percutaneous puncture (ABEATICI & CAMPI 1951; LEGER et coll. 1951). After discussion of the terminology GVOZDANOVIĆ & HAUPTMANN (1955) called this method percutaneous lieno-portal venography.

3. After percutaneous puncture of a large portal branch near the hilum of the liver — percutaneous transhepatic portal venography (STEINBACH et coll. 1953).

4. The demonstration of the splenic and portal veins is also possible after injection of the contrast medium from the arterial side, as is done in abdominal aortography. ÖDMAN (1956) catheterized the coeliac artery to obtain a more selective filling of the portal system.

Of these methods for the roentgenographic investigation of the portal system, percutaneous lieno-portal venography has been most widely used.

Technique. Two main techniques have been used for percutaneous puncture. In the more common method, the contrast medium is not injected until the examiner has

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convinced himself that the tip of the needle is in correct position in the splenic parenchyma, during which period shallow breathing is allowed. This method was described in detail by BOULVIN et coll. (1951) and has since been used by DE SCOVILLE & LEROUX (1952), SCHOLZ et coll. (1954), ATKINSON et coll. (1955), FIGLEY et coll. (1955) and LEGER (1955). In the other method, the contrast medium is injected immediately after splenic puncture, and the patient is not allowed to breathe as long as the tip of the needle is in the spleen. This method, which is believed to decrease the risk of splenic injury, has been used by DREYER & BUDTZ-OLSEN (1952), COOPER et coll. (1953), GVOZDANOVIĆ et coll. (1953, 1955), KONAR & SEN GUPTA (1953) and BERGSTRAND & EKMAN (1955).

FERNSTRÖM (1955) and BERGSTRAND & EKMAN (1955) described methods with percutaneous introduction of a flexible plastic catheter into the spleen to permit repeated injections of contrast medium with the patient in different postures. WANNAGAT (1955, 1956) recommended puncture of the spleen under laparoscopic control in order to diminish the risk of complications. On the basis of experience gained in the puncture of the spleen from the side with the needle in a frontal plane several authors recommend the examination only if the spleen is enlarged (SCHOLZ et coll. 1954 and ATKINSON et coll. 1955). Spleens of normal size were punctured with the needle in a sagittal plane and inserted along the longitudinal axis of the spleen (LEGER et coll. 1953; LEROUX & DE SCOVILLE 1954). After roentgenographic indication it was possible to puncture even the normal-sized spleen from the lateral side (BERGSTRAND & EKMAN 1955).

The puncture is generally made under local anesthesia. In most series on record the amount of contrast medium injected varies between 20 and 50 ml diodone 70 %. In order to secure a sufficiently high concentration of the contrast medium in the venous pathways with manual injection it is necessary to use a cannula with an outer diameter of at least 1.5 mm.

Most investigators, *e. g.* LEGER (1955), carried out percutaneous lieno-portal venography with 1 to 3 exposures. GVOZDANOVIĆ et coll. (1953, 1955), BERGSTRAND & EKMAN (1955, 1957) stressed the value of a larger number of serial films for the study of the vascular pattern of the liver and of the hemodynamics in the portal system. ATKINSON et coll. (1955) used a biplane procedure.

Complications. The most serious complication of percutaneous lieno-portal venography is intra-abdominal hemorrhage. Laparotomy after the examination has revealed quantities of blood of anything up to 100 ml around the spleen (COOPER et coll. 1953; SCHOLZ et coll. 1954; BERGSTRAND & EKMAN 1955; GVOZDANOVIĆ & HAUPTMANN 1955). However, hemorrhage with clinical signs after percutaneous lieno-portal venography appears to be rare. Thus LEGER 1955 (more than 200 examinations) and PEDRO-BOTET 1956 (100 cases) observed no such complications. FIGLEY et coll. 1955 (150 compilated examinations) and GVOZDANOVIĆ & HAUPTMANN 1955 (61 examinations) reported hemorrhage with clinical signs in a total of 3 examinations. In a few small series, especially of splenic puncture at laparotomy, however, a high frequency of intra-abdominal hemorrhage has been reported (DU BOULAY & GREEN 1954; KEMP HARPER 1955; REYNOLDS et coll. 1955). Extra-splenic deposition of contrast medium into the abdominal cavity or adjacent organs (stomach, colon and pleura) is not uncommon but does not produce any serious sequelae.

Indications and diagnostic possibilities. The most common indication for percutaneous lieno-portal venography has been investigation of probable portal hypertension (DOGLIOTTI & ABEATICI 1954; LEBON et coll. 1954; ATKINSON et coll. 1955; BERGSTRAND & EKMAN 1955; LEGER 1955).

The hemodynamics of the portal system has been studied in the presence and absence of portal hypertension and in animal experiments (BERGSTRAND & EKMAN 1957). The

results showed that the rate and direction of the circulation and the width of the vessels can be determined by percutaneous lieno-portal venography; the injection of contrast medium will consequently not increase the portal pressure. The determination requires an automatic, rapid exchange of films under standardized conditions. Since the blood flow is not always directed towards, or does not always reach, an organic portal obstruction, the exact site of the obstruction cannot always be determined, in contrast to what was formerly claimed (DREYER 1954; ATKINSON et coll. 1955; BERGSTRAND & EKMAN 1955; FIGLEY et coll. 1955; GVOZDANOVIĆ & HAUPTMANN 1955).

In studying the passage of the contrast medium for 30 to 40 sec after the injection it was possible to demonstrate the accumulation of contrast medium in the liver parenchyma and the hepatic veins (LEBON et coll. 1954; BOURGEON et coll. 1954; BERGSTRAND & EKMAN 1955).

Percutaneous lieno-portal venography has also been found useful in the investigation of tumours of the liver and pancreas (COOPER et coll. 1953; LEGER 1953, 1955; LEROUX & DE SCOVILLE 1954; BERGSTRAND & EKMAN 1955).

Own investigations

The most important factors to be considered in percutaneous lieno-portal venography are discussed on the basis of all such examinations performed in our Roentgendiagnostic Department.

The material consisted of 175 examinations carried out during a 3-year period (November 1953 to October 1956) on 128 patients, aged 2 to 78 years, the majority (70) being between 46 and 65 years of age. The examinations, listed according to the conditions in the portal system as judged by percutaneous lieno-portal venography and clinical examination (including laparotomy, biopsy and/or autopsy), were as follows: Twenty-two (22) examinations were performed on normal subjects, 31 on patients with expansive processes, 63 on patients with liver cirrhosis, 34 on patients in whom a porta-caval shunt had been established, 14 on patients with extrahepatic thrombosis and 11 on patients with miscellaneous diseases (hemolytic anemia — 2, myelofibrosis — 3, malformations — 5, chronic hepatitis — 1). Twenty-one of the examinations were unsatisfactory.

Most of the patients were in a poor general condition. Thus 36 patients with liver cirrhosis had jaundice and/or ascites indicating severely impaired liver function; 56 examinations were carried out on these patients. In 148 examinations the coagulation of blood was determined using the prothrombin index according to Quick. The prothrombin index was found to be reduced (30—59) at 21 examinations, slightly reduced (60—79) at 84, and normal (80—110) in 43.

Technique. All of the examinations were made in the fasting state after the bowels had been thoroughly cleared. Provided renal function was satisfactory, the patient was tested for any hypersensitivity by the intravenous injection of 1 ml contrast medium at least one hour before the examination. The patients were premedicated with morphine-scopolamine or Pentobarbital sodium and the pulse rate and the blood pressure were noted about one hour before the examination.

The site of the spleen was indicated on the skin with the patient in the position (supine, except in 3 cases in which the position was prone) and the respiratory phase in which the examination was to be carried out. It was possible to judge the size of the spleen in the conventional roentgenograms obtained (BERGSTRAND & EKMAN 1957).

Local anesthesia was used except in 8 cases, mostly children, where general anesthesia was used.

In 172 examinations the spleen was punctured with a cannula, 10 cm long and of 1.5 mm outer diameter. In 35 of these the cannula was provided with a mandrin. In 3 examinations the spleen was punctured with a plastic catheter (outer diameter 2 mm) provided with a metal tip and threaded on a rigid guide. In 148 examinations the contrast agent used was sodium acetrizoate 50 % (Triurol) — and in 27 diodone 50 % (Umbradil).

The spleen was punctured with the needle in a frontal plane at the level of the posterior axillary line or, if the patient had splenomegaly, somewhat more ventrally. The cannula was introduced until its tip was felt to scratch the rough surface of the spleen. Sometimes, however, it was not possible to elicit this important sign which indicates that the needle lies in the correct direction. During apnoea the cannula was then introduced rapidly towards the hilum of the spleen to a depth of 2 to 4 cm depending on the size of the organ.

Two different injection methods were used:

1. Blind injection of contrast medium: In 137 examinations, in which the spleen was punctured during the inspiratory phase, the contrast medium was injected immediately.

2. Controlled injection of contrast medium: In 35 examinations the spleen was punctured in the resting respiratory state with a cannula provided with a mandrin. If the tip of the cannula was in the spleen it would swing to and fro with the shallow respiration allowed, and drops of blood would flow from its free end, though sometimes not until the position of the needle had been slightly changed. Not until blood had begun to flow from the tip of the needle was the contrast medium injected during apnoea; this was usually effected within one minute after splenic puncture.

The contrast medium was injected by hand. The rate of injection was < 6 ml/sec in 16 examinations, 6 to 7.5 ml/sec in 145 examinations, and 10 ml/sec in 14 examinations. On conclusion of the injection the cannula was immediately withdrawn from the spleen. In 164 examinations, the amount of contrast medium injected was 30 ml and in 11 examinations (mostly of children and patients in the early part of the material) 6 to 20 ml per injection. Only in 4 examinations did the patient receive more than one injection of contrast medium.

Roentgen technique. One hundred and forty-nine (149) examinations were performed with an Elema film changer, which permits a wide variation in the number and frequency of exposures. In 35 of these examinations the passage of the contrast medium was studied only during 5 to 15 seconds after the beginning of the injection. Twenty-five (25) of these, however, were performed on patients with a porta-caval shunt. In 31 examinations the passage of the contrast medium was studied for 16 to 25 seconds, in 77 for 26 to 35 seconds and in 6 for more than 35 seconds after the beginning of the injection. In the majority of the examinations the frequency of exposures was 1 per second for 10 to 13 seconds, and then 1 every third second for the rest of the examination. Exposure data: 70 to 105 kV, 500 mA, and 0.06 to 0.20 sec; focus: 2×2 mm. F. F. D. 90 cm; Patterson high-speed intensifying screens, cross-grid, filter 3 mm Al (effective).

Examination of many of the patients was often technically difficult because of ascites. The quality of the radiation necessary for obtaining assessable films with short exposures did not involve any disturbing increase in the scattered radiation. The skin dose calculated from exposure data varied usually between 25 and 40 r per 25 exposures.

On an obese patient weighing 98 kg examined in one plane with a series of 26 exposures the dose as measured by ionisation chambers on the skin 56 cm from the focus was found to be 36 r.

The calculated geometric enlargement of the splenic vein and the portal vein in examinations in the supine position was about 25 per cent provided that the vessels are situated 18 to 20 cm from the film, which was found to be the case in measurements of 5 cadavers of ordinary size and body-build.

In the first part of the material 17 examinations were performed with an older type of automatic casette changer permitting 10 exposures in 14 seconds and 9 with manual changing of 3 casettes during 6 to 8 seconds. Biplane examinations were only used in 2 examinations because of the disadvantages of scattered radiation.

The genital organs were always well shielded against radiation. The examiner was protected from radiation by a lead screen.

After the series of exposure had been made, a film was taken of the spleen in order to judge the degree of any extra-splenic deposition of contrast medium. The blood pressure and pulse rate were compared with the values obtained before the examination and they were checked for the first few hours afterwards. In the latter half of the material, the patients were instructed to lie on the left side for 4 to 5 hours after the examination.

Results

Provided that the tip of the needle was in the splenic parenchyma, the contrast medium flowed into the venous pathways as long as contrast medium was injected, but in a varying proportion according to the injection technique employed. In 131 of the 175 examinations the entire amount of contrast medium injected passed into the veins. In 23 examinations part of the contrast medium was deposited outside the spleen, often because of backflow during the injection, and in 21 the entire dose was deposited extralienally.

It was believed that the factors mainly responsible for extravascular deposition of the contrast medium should be sought in 1) the injection method, 2) the rate of injection, and 3) the size of the spleen.

1. Injection method: Of 137 examinations with *blind injection* of the contrast medium, the entire dose was deposited intravascularly in 110. In 10 examinations only part of the contrast medium was deposited intravascularly. In 2 of these, the examination had been preceeded by an unsuccessful attempt to introduce a plastic catheter. The contrast medium was deposited extravascularly in 17 examinations. (13 of these were performed on patients with a normal-sized spleen.) In 4 of them the tip of the needle was probably situated lateral to the spleen. 2 of those patients who died from their liver disease within 2 months were examined post mortem; ascites and pronounced fibrotic thickening of the splenic capsule, in one combined with calcifications, were present. In 6 examinations the tip of the needle as judged from the frontal film, was situated too far medially. In 4 the contrast medium had been injected

too far cranially, in 3 of these into the left pleura. In the remaining 3 examinations the entire dose of contrast medium was deposited extralienally despite the fact that the position of the needle seemed to be correct. In one of these the spleen was enlarged.

Of 35 examinations with *controlled injection* of contrast medium the entire dose of contrast medium was deposited intravascularly in 19. In 13 examinations only part of the contrast medium was deposited intravascularly; in 2 of these examinations, which were carried out on dyspnoic patients, pronounced respiratory excursions were observed, while the tip of the needle was in the spleen. The contrast medium was deposited extravascularly in 3 examinations. In 2, the tip of the needle was situated too far medially or cranially. In the third case, in which the spleen was enlarged, the entire dose was deposited extralienally though the needle as judged by the frontal film was in the correct position.

2. Rate of injection: Two groups of examinations, comparable regarding injection method and spleen size, were analysed for any influence of the rate of injection of contrast medium. In one group (16 examinations) where a low injection rate (< 6 ml/sec) was used the entire dose of contrast medium was deposited intravascularly in 15, and entirely extralienally in 1. In the other group (14 examinations) with a high rate of injection (10 ml/sec) the contrast medium was deposited entirely intravascularly in 10, partly in 3, and entirely extralienally in 1. Thus the frequency of extralienal deposition of contrast medium did not appreciably vary with the rate of injection.

3. Size of spleen: Regardless of the method of injection the risk of the entire dose of contrast medium being deposited extralienally was obviously greater in patients with a spleen of normal size than in those with splenic enlargement (14 of 70 and 7 of 105 examinations, respectively).

Comments. Extrasplenic deposition of contrast medium is due above all to an incorrect position of the tip of the needle, the risk being greater if blind injection is performed in patients with normal-sized spleens and with thickening of the splenic capsule. Fuld & Irwin (1954) sometimes observed that the spleen moved about 5 cm medially before the needle point entered the splenic capsule.

The possibility of performing controlled injections with a needle without complications has diminished the necessity of the somewhat more tedious examination with a plastic catheter. However, the plastic catheter permits repeated injection of contrast medium with the patient in different postures, an advantage that should not be underestimated.

Ekman (1957) measuring intrasplenic pressure observed that the manometer level often drops from intrasplenic level to intra-abdominal within 10 to 30 seconds. This was explained by increasing leakage along

the puncture canal. In order to avoid such a reflux of contrast medium the needle should be in the spleen as short a time as possible. The use of controlled injections should, owing to the longer time the needle is in the splenic parenchyma, probably be limited to examinations of patients with a normal-sized spleen.

Intrasplenic injection. Of 131 examinations, in which the entire dose of contrast medium had been deposited into the spleen, the contrast density as seen in the roentgenograms was good in 106 and less good in 25. It was presumed that the vascular contrast density depends on the concentration of the contrast media, the rate of injection and the dilution in the vessels, which varies with the velocity of flow and width of the vessels. Thus, in view of the many factors possibly influencing contrast density the present material was not large enough to permit a separate discussion of each.

Triurol, which contains 32 per cent more iodine than Umbradil (ODÉN 1955) naturally produced a good contrast density more frequently than Umbradil (96 of 111 and 10 of 20 examinations, respectively). The relatively moderate variation in the rate of injection (from 5 to 10 ml/sec) had no appreciable influence on the contrast density recorded.

Low contrast density was noted more frequently in examinations of patients with a functioning porta-caval shunt than in the remainder (15 of 27 and 10 of 104 examinations, respectively). The results may be explained by EKMAN's observation (1957) that velocity of flow increases after porta-caval shunt but the widening of the vessels persists unchanged.

Owing to the relatively high specific gravity of the contrast medium, it usually filled the declival parts of the portal system better and earlier than the remainder. Thus, in examinations in the supine position the vessels in the ventrally located left lobe were less well filled than in examinations performed with the patient in the prone position. A patient who at laparotomy showed signs of extra-hepatic block, was examined both in the supine and in the prone position. In the latter a good filling was obtained of the splenic vein, the proximal portion of the portal vein, and the coronary vein. On examination in the supine position a filling was obtained of only the dorsally located splenic vein and the short gastric veins.

It seemed evident that the distribution of the contrast medium also varies with the amount of contrast medium injected and with the portal vascular volume. We found a dose of 30 ml to be suitable for adults.

Evaluation of the portal circulation. In patients with a patent passage to the liver the contrast medium flowed through the splenic vein and the portal vein to the liver parenchyma at a rate varying with the presence and extent of portal stasis. The accumulation of contrast medium in

the liver parenchyma varied in relation to the amount of contrast medium passing through the sinusoides. As the accumulation of contrast medium gradually diminished, the hepatic veins appeared in the films, though with low density, demonstrable especially in healthy subjects and in patients with liver metastases. The successively decreasing accumulation of contrast medium in the liver parenchyma persisted after the appearance of the hepatic veins.

In those examinations in which the entire amount of contrast medium injected (30 ml Triurol 50 %) passed through the liver, the interval between the beginning of injection and the disappearance of the contrast medium from the liver parenchyma was determined. About 28 seconds after the beginning of the injection (10 assessable examinations) the accumulation of the contrast medium in films as compared with films without any contrast medium in the liver was good in 2, less good in 5, and slight in 3. About 31 seconds after the beginning of the injection (7 assessable examinations) the accumulation of the contrast medium was less good in 3 and slight in 4. About 34 seconds after beginning of the injection, the accumulation of contrast medium was slight in 2 assessable examinations. In none of the 84 examinations of patients with collateral circulation were the collaterals demonstrable for more than 25 seconds after the beginning of the injection. In 29 examinations of patients with functioning porta-caval shunt the contrast medium disappeared from the vessels within 8 seconds after the beginning of the injection. Thus serial films taken during a period of about 35 seconds after the beginning of the injection were necessary for evaluation of all phases of the passage of contrast medium. In the evaluation of the function of a porta-caval shunt, however, films taken for 6 to 10 seconds proved sufficient.

The results in the latter part of the material concerning the frequency of exposures necessary for assessing the velocity of flow in the splenic vein and the portal vein agreed with that found earlier in an investigation consisting of 115 examinations in the former part of the material (BERGSTRAND & EKMAN 1957). For determination of the rate of circulation in the portal system it was necessary to use automatically changed films with a frequency of one per second during the first 13 seconds and then one every third second for the following 20 seconds.

Reactions and complications

The premedication and the local anesthesia employed were sufficient to inhibit pain during splenic puncture. A sensation of warmth or burning during injection localized to organs perfused with the contrast medium, was common. In 6 examinations, in 5 of which the patients had liver metas-

tases, the patient complained of pain in the right hypochondrium during and for a few minutes after the injection of the contrast medium. Pain of varying intensity in the left side or left shoulder during and after the injection and with a duration from half an hour to one day was noted after 36 of 167 examinations carried out under local anesthesia; only in 3 of them was the contrast medium deposited entirely intravascularly. In 131 examinations, the patients reported slight pain at the site of puncture. In 120 of them the contrast medium was deposited entirely intravascularly, in 3 the entire dose was deposited extralienally, in 2 of them into ascitic fluid in the abdominal cavity, and in 1 into a hypernephroma near the spleen. Most of the patients felt tired some hours after the examination without any deterioration in their general physical condition. Patients with jaundice and/or ascites suggesting marked impairment of liver function did not react in any different way. These reactions occurred regardless of choice of pre-medication and contrast medium. Unlike Pentobarbital sodium, morphine-scopolamine often made it difficult for those patients with poor liver function to co-operate satisfactorily during the examination.

The blood pressure was, as a rule, somewhat increased after the examinations. In 15 examinations in most of which contrast medium had been deposited extralienally, the blood pressure dropped by more than 20 mm Hg and nausea usually occurred. After 4 of the 175 examinations (3 belonging to the earlier part of the material) the patients showed signs of shock and abdominal pain suggesting intra-abdominal hemorrhage. Three examinations were carried out in patients with portal hypertension and splenomegaly due to liver cirrhosis and 1 in a patient with bronchial cancer and liver metastases who had a normal-sized spleen. Three of the examinations were performed in the supine position with blind injection of the contrast medium (of which 1 was performed after an unsuccessful attempt to introduce a plastic catheter) and 1 with controlled injection of contrast medium in the prone position. In this case — the patient with bronchial cancer – deep breathing was observed during the examination. Liver function was markedly reduced in 2 and slightly reduced in 1 of the patients with liver cirrhoses. The prothrombin index was 60, 61, 78 and 81, respectively. In 2 of the patients the bleeding time, the coagulation time, and number of thrombocytes were determined and all found to be normal. Shock was regularly controlled by transfusion of blood or Dextran N. N. R. In 1 of the patients with cirrhosis a porta-caval shunt was performed 4 days later; no signs of intra-abdominal bleeding were then observed. The other 2 patients showed further impairment of liver function after the hemorrhage. The patient who had liver metastases and who was in a poor general condition before the examination died 10 days afterwards. Post-mortem examination showed

signs of only slight fresh bleeding in the abdominal cavity. Most of the patients with liver cirrhosis in the present material were operated on one to two weeks after the examination. In none were any signs of serious, intra-abdominal hemorrhage observed.

An elevation of temperature, in most cases moderate, was registered up to one week after about 10 examinations. Some hours after the examination with Triurol one patient had urticaria and Quinke edema. One month later percutaneous lieno-portal venography was performed with Umbradil without any untoward reaction.

To sum up, in investigations without extralienal deposition of contrast medium, the patient showed no untoward reaction except a certain sensation of burning during the injection of the contrast medium. In examinations in which contrast medium was deposited extralienally the patients complained of pain in the left flank or the left shoulder, usually varying in intensity and duration with the amount of contrast medium deposited extralienally. In some cases, a marked decrease in the blood pressure occurred with slight nausea. After 4 of the 175 examinations, the patients showed clinical signs of intraperitoneal bleeding without any demonstrable relation to the prothrombin index, the injection method, or the size of the spleen.

Comments. Many authors warn against percutaneous lieno-portal venography of patients with decreased clotting power and/or normal-sized spleen (Scholz et coll. 1954; Atkinson et coll. 1955; Gvozdanović & Hauptmann 1955). The 4 patients in the present material who showed clinical signs of intra-abdominal bleeding had only a moderate reduction in the coagulability of the blood as measured by the prothrombin index. None of the patients belonged to the group with a prothrombin index of less than 60.

Even if the risk of extralienal deposition of contrast medium and thereby of pain is greater in examinations of patients with a normal-sized spleen, the method with controlled injection of contrast medium does not appear to imply any increased risk of bleeding, an observation in contradiction to earlier suggestions (Bergstrand & Ekman 1955; Gvozdanović & Hauptmann 1955). The possible risk of splenic lesions has, however, induced us to refrain from the use of repeated injections with the patient in different postures with the needle in position for such a long time. Instructing the patient to rest on the left side after the examination might imply a certain degree of mechanical compression at the site of the puncture in the spleen and thereby explain the decreased frequency of bleeding in the latter part of the material.

Although the material was to a large extent made up of patients with markedly impaired liver function, no signs of untoward effect on the liver were noted in association with the injection of contrast medium.

The increase in pressure in the portal system 30 seconds to 1 minute after percutaneous lieno-portal venography, observed in human beings by Le Go (cit. Leger 1955) and in dogs by Bergstrand & Ekman (1957), however, suggest that injection of the contrast medium might have some effect on the liver. This assumption is also strengthened by the pain in the region of the liver described by some patients during and after the injection of the contrast medium.

Conclusions

On analysis of results and complications of 175 percutaneous lieno-portal venographies performed by different techniques in 128 patients, several with severely impaired liver function and reduced prothrombin index, the following observations were made:

1. Signs of shock and abdominal pain suggesting intra-abdominal hemorrhage were noted after 4 examinations.
2. The risk of intra-abdominal hemorrhage did not appear to vary with the size of the spleen or the prothrombin index.
3. As compared with blind injection of contrast medium controlled injection did not increase the risk of intra-abdominal hemorrhage but decreased the risk of extrasplenic deposition of contrast medium in patients with a normal-sized spleen.

Thus, percutaneous lieno-portal venography, with the technique used, gives valuable information on the morphology and hemodynamics of the portal system without any undue risk of complications.

SUMMARY

An analysis is given of the results and complications of 175 percutaneous lieno-portal venographies performed by different techniques in 128 patients.

ZUSAMMENFASSUNG

Die Ergebnisse und Komplikationen von 175 perkutanen lieno-portalen Venographien, mit verschiedener Technik in 128 Patienten ausgeführt, werden analysiert.

RÉSUMÉ

Les résultats et les complications de 175 veinographies spléno-portales percutanées, faites par des techniques différentes dans 128 cas, sont analysés.

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ROENTGENOGRAPHIC CHANGES IN THE LUNGS AND VERTEBRAE FOLLOWING INTENSE ROTATION ROENTGEN THERAPY OF ESOPHAGEAL CANCER

by

Karl-Eric Borgström and *Inge Gynning*

In radiotherapy of intrathoracic esophageal tumours aiming at a curative effect the possibility of radiation reactions in the lungs and in the thoracic vertebrae at the level of the tumours must be taken into account, independently of the technique used. Such changes also occur after moving beam therapy despite the relatively favourable distribution of the dose.

This paper is concerned with the frequency and appearance of radiation reactions in the lungs and vertebrae of 143 patients who had received rotation roentgen therapy in a single course during the years 1944—1952.

Treatment was uniform throughout the period under consideration. The patient was placed in a revolving chair with the arms upstretched and the hands resting on a trapeze. He was fixed by means of a band around the upper part of the thorax and another around the legs below the knees. Focus-rotation centre distance 53 cm, focus-fluorescent screen distance 106 cm; 170 kV, 15 to 20 mA; 0.5 mm Cu + 1 mm Al filtration. As a rule the breadth of the field in the plane of the tumours was 5 to 6 cm. Continuous fluoroscopic control was carried out from an adjacent observation cabin, from which the diaphragm was also manipulated. The dose in the region of the tumours was regularly measured with a chain of 2 to 8 Sievert's ionisation chambers passed down the esophagus with the aid of a rubber or plastic catheter. The position of the chambers in the region of the tumours was checked with the aid of indicators and

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special arrangements on the screen. The daily tumour dose was 200 to 225 r. The total tumour dose was usually kept between 6,000 and 6,500 r spread over 35 days, which as a rule proved necessary for a curative effect on squamous cell cancer of the esophagus. In an attempt to determine the optimal dose both under- and over-dosage occurred, the latter being followed by complications from the esophagus and neighbouring organs. Treatment was thus not entirely uniform. This provided a better opportunity to detect and study factors capable of favouring the occurrence of radiation changes.

Lungs. Reports are available of investigations carried out to assess the influence of different doses delivered under varying conditions to different kinds of animals (2, 15, 16, 23).

Untoward reactions of the lung to roentgen irradiation was first described by HINES in 1922 and soon afterwards by GROOVER & coll. (10, 8). Since then many case reports have been published. Most of these were on postoperatively irradiated mammary cancer and on intrathoracic tumours treated with large doses. WARREN and SPENCER (24) described an unselected autopsy series, where 12 per cent of 234 subjects that had received roentgen therapy had radiation reactions of the lungs. Untoward reactions of the lungs following irradiation of esophageal cancer have been described by ENGELSTAD (4), STRANDQVIST (20), and others who have used stationary fields. LEACH (13) studied lung function in patients who had received unilateral irradiation of the lung and found considerable changes in pulmonary function on the irradiated side. This is, of course, the best measure of the degree to which a lung has been affected by irradiation. No such examinations were carried out in the present investigation, the cases being judged solely on the basis of roentgen findings and clinical data. A fairly thorough search of the literature failed to reveal more than a few single case reports of roentgenographic changes in the lungs following moving beam therapy of intrathoracic tumours. A few cases were accounted for by J. NIELSEN (17) in a series of 194 cases where the total dose lay between 4,000 and 5,000 r. SCHNEIDER (18) reported 1 case after pendular irradiation.

In the investigations referred to above the changes were observed mainly in the lung parenchyma but were also seen in the bronchi, pleurae, and mediastinum. In the present investigation reactions were encountered only in the lungs. On no occasion did we observe exudate or other pleural changes ascribable entirely to the treatment. Systematic roentgen examinations with the patient in the lateral position were carried out for one year. Bronchography was considered contra-indicated.

In his papers published during the nineteen-thirties ENGELSTAD (2, 3, 4) gave a good description of the microscopic picture during different stages of radiation reaction of the lung as well as of the clinical course.

Since we gave only relatively small daily doses, primary reactions were observed clinically but rarely roentgenologically. ENGELSTAD's third stage with inflammatory changes was occasionally observed in patients who had received a much larger dose than what we now consider optimal. As a rule we were only able to demonstrate his Stage 4, *i. e.*, fibrosis, which is due to an increase in the interstitial connective tissue of the lungs.

Rotation therapy delivers the largest dose to the esophagus and its immediate surroundings. Outside of this core the dose gradually decreases, so that it is considerably smaller in the periphery of the lung. This gives the fibrosis a characteristic roentgenographic appearance.

As a rule the changes are bilateral and are most marked close to the esophagus. They decrease in height and density peripherally. In tumours in the lower portion of the esophagus the changes in the left lung were somewhat more marked because of the curved course of the esophagus and consequent necessity of using a relatively broad field. Slight fibrosis is the most common sequela. This is best observed in lateral views. If the fibrosis is severe, the roentgenogram will show a massive central density decreasing peripherally. Between these two extremes the changes vary in intensity from one case to another. In cases that have been followed up for several years a considerable tendency to shrinkage was observed. In none of the stages was the extent of the fibrosis limited by the borders of the lobes, an observation which might be of differential diagnostic value.

The changes were never classified as fibrosis before the patients had been followed up for at least 4 months. Of all 174 patients 143 were completely treated and in these cases roentgenograms of the chest were taken routinely before, during and after treatment. In 38 of the 57 cases with intrathoracic changes these were ascribed to roentgen therapy. Of the remaining 19 patients, 6 had lung metastases. In addition pneumonia, aspiration changes, and progression of earlier tuberculosis were noted. Four patients had lung changes in association with inflammatory perforating processes of the esophagus.

Of 38 patients with radiation reactions 30 were examined regularly during the course of treatment, at the end of the treatment, and once every other month afterwards. In these 30 patients the lung changes in 22 were demonstrated within 4 months of the beginning of treatment. Fifteen cases were diagnosed between the second and third month. In only 3 were the changes observed after more than 7 months. In half of the patients with fibrosis and surviving more than one year fibrosis had gradually increased.

Only in 3 cases were marked changes observed initially. These patients, who had been irradiated with unusually broad fields (more than 6 cm)

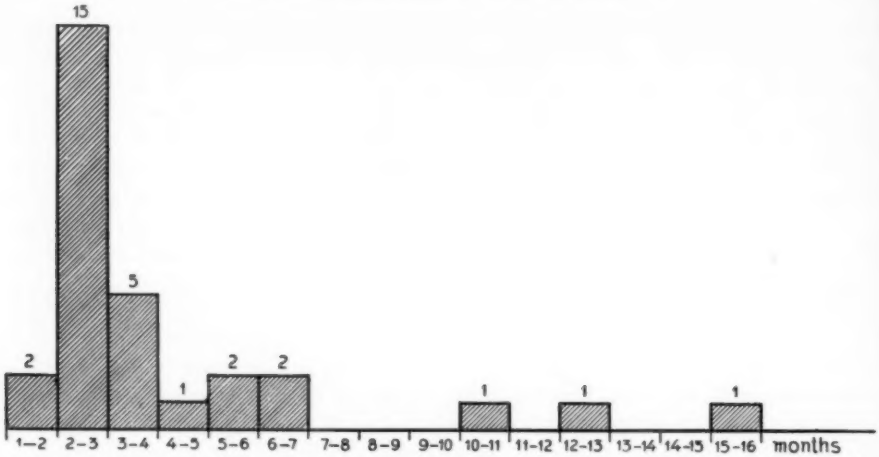

Diagram 1. Interval between beginning of treatment and appearance of lung fibrosis.

and very large doses, died from complications of overdosage. Two of them had from the beginning marked atelectasis, which afterwards disappeared. These changes which occurred soon after treatment were judged as primary reactions.

Symptoms of primary roentgen reactions of the lung and bronchi were noted during and for the first few months after treatment in the form of a usually mild cough. This often occurred even in the absence of radiographically demonstrable fibrosis or other radiation reactions.

Symptoms of roentgenologically manifest lung fibrosis are more difficult to evaluate unless lung function has been studied before and after treatment. As a rule the patients are old (mostly 65 to 70 years of age) and cardiac function somewhat impaired, so that it is sometimes difficult to judge the primary origin of the symptoms. Only in 3 cases that had been followed up for a long time was a continuous cough and shortness of breath noted. These patients were also troubled by a viscous expectorate. In the other cases where a cure of several years was obtained the fibrosis usually produced no symptoms.

It appears that occurrence of fibrosis of the lung is due mainly to two factors: the size of the dose and the breadth of the field in the rotation centre. The following factors may also play a contributory role: Advanced age with degenerative changes of the heart and vessels; poor general physical condition with low serum albumin as signs of the poor nutritional state; earlier or existent pulmonary affections such as tuberculosis, chronic bronchitis, and the like. The occurrence of unknown individual factors cannot be excluded either.

The maximum tumour dose was high in practically all the cases of fibrosis. As a rule the calculated maximum dose lay between 6,400 r spread over 34 days and 6,800 to 6,900 r spread over 39 to 40 days. In some cases a dose of more than 7,000 r was delivered within this period, which, judging from our experience, is too large.

Table 1

Breadth of field	Patients without fibrosis and followed up for at least 1 year Number of cases	Patients with fibrosis Number of cases
4 cm	3	—
5 »	9	3
6 »	15	22
7 »	8	13
	35	38

The significance of the breadth of the field for the development of lung fibrosis is apparent from Table 1, where it is seen that fibrosis was more common in cases in which a broader field had been used.

On the 31 May 1956 it could be stated that of the 143 patients completely treated by the rotation method a 3-year/cure had been obtained in 19, a 5-year-cure in 12, and a 10-year-cure in three. In 10 of these 19 cases fibrosis of the lung was demonstrated. Thus if curative effect is to be secured, fibrosis is difficult to avoid.

Vertebrae. The literature of this subject is rather meagre excepting for case reports of roentgen reactions, particularly in the pelvis and the neck of the femur after treatment of cancer colli uteri and epiphyseal injury in growing individuals. A fairly thorough search failed to reveal any data on roentgen reaction of the vertebrae to rotation therapy of esophageal cancer. This might be explained by the lack of large materials with sufficiently long survivals for demonstration of such skeletal changes. Another condition for the demonstration of the changes is that lateral views be taken routinely during follow-up studies of the esophagus and lungs.

Radiation changes of the vertebrae were seen in 13 cases; in 3 of these only the vertebrae were involved, while in 10 co-existent pulmonary changes were present. The breadth of the field in the above-mentioned 3 cases was less than 6 cm, while in the other 10 it was 6 to 7 cm. The maximal tumour dose in these two groups was about the one we consider optimal, namely 6,500 r over 35 days; in some cases, however, it was larger. The tumour was situated in the middle portion of the esophagus where the distance between the esophagus and the vertebrae is smallest. Roentgenographically the changes appeared as osteoporosis with compression

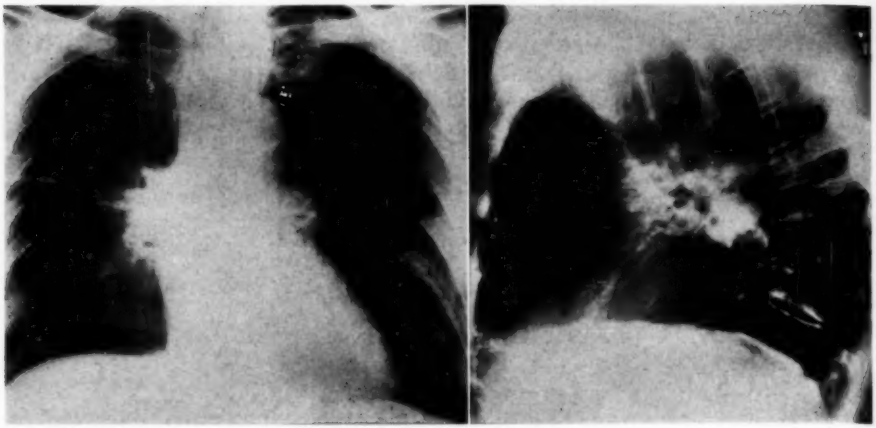

Fig. 1. 11-year-cure of microscopically verified esophageal cancer with lung fibrosis.

of the vertebral body. Only in 1 case did the vertebral changes appear within one year. In all the others they arose later, 6 between 1 and 2 years, 3 between 3 and 4 years, and 3 between 5 and 9 years. The vertebral changes thus appear much later in the roentgenogram than the changes in the lung. None of the patients with bone involvement had any appreciable symptoms referable to the back, the vertebral changes being noted as incidental findings during follow-up. The relationship between the healing of cancer and the occurrence of vertebral changes is also evident from the fact that as many as 12 of the 19 patients who survived more than 3 years had vertebral compression. It is thus apparent that the large tumour dose and the proximity of the vertebrae to the tumour are the main causes of radiation changes which usually do not appear until one year after treatment and often later. All these observations may be exemplified by the following case of typical marked lung fibrosis with vertebral compression.

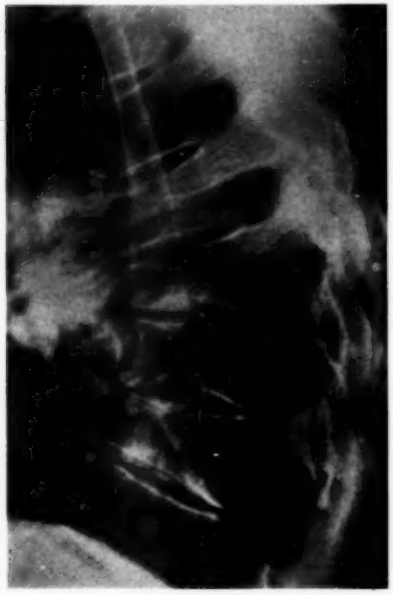

Fig. 2. Same case. Compression of several vertebrae.

A man, aged 70, with a tumour 8 cm long in the middle portion of the esophagus received a very large maximum dose, about 6,700 r spread over 28 days which, according to STRANDQVIST (21), corresponds to 6,900 r spread over 35 days; field breadth 7 cm. Typical lung fibrosis developed, most marked centrally, with compression of several vertebrae. He is still alive, 11 years after treatment, without back or pulmonary symptoms. The lung fibrosis developed 9 weeks after treatment but the vertebral compression did not occur until 3 years later (Figs. 1 and 2).

Conclusion

Of 143 cases of esophageal cancer treated by the rotation roentgen method with a large total tumour dose aiming at a curative effect, lung fibrosis occurred in 38, in 10 of which vertebral compression was also noted. In 3 cases vertebral changes were the only reactions observed. As a rule the lung changes appeared between the 2nd and 3rd month after the beginning of treatment, the vertebral changes not occurring until after the second year. Of the 19 patients who had survived for at least 3 years, more than half had pulmonary and vertebral changes. A large total tumour dose is the main cause of these changes; as to lung fibrosis, the breadth of the field is also of importance. In most cases the patients had no or only slight symptoms due to the alterations described and their occurrence does not seem to contra-indicate the use of the tumour doses suggested by us. With technical improvement permitting irradiation with narrower fields and more homogeneous distribution of the tumour dose it will probably be possible to reduce the frequency and extent of lung fibrosis following rotation roentgen therapy of esophageal cancer.

SUMMARY

A description is given of the frequency, cause, and clinical significance of lung fibrosis and vertebral changes in 143 cases of esophageal cancer treated by the rotation roentgen method.

ZUSAMMENFASSUNG

Die Häufigkeit, die Ursache und die klinischen Merkmale der Lungenfibrose und der Wirbelkörperveränderungen in 143 mit der Röntgenrotationsmethode behandelten Fällen mit Ösophaguskarzinom werden beschrieben.

RÉSUMÉ

Sur 143 cas de cancer de l'oesophage les auteurs ont étudié la fréquence, la cause et l'importance clinique de la fibrose pulmonaire et des lésions vertébrales dues à la roentgenthérapie rotatoire.

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EXPERIMENTAL MICRO-LYMPHANGIOGRAPHY

by

Sven Bellman and *Bo Odén*

It has long been possible to obtain angiograms of lymph vessels, both in experimental animals and in man. Lymphangiograms have often been obtained inadvertently in roentgenographic examinations in which contrast media have been employed. This has been the case especially in hystero-salpingography (14, 39, 13), occasionally in examinations of the nasal sinuses (35), in myelography (25), and in retrograde pyelography (1). The generally accepted explanation of these phenomena is that the contrast medium has been introduced directly into abnormal lymph vessels communicating with the investigated lumen as a result of disease or of traumatic rupture during the injection. Another factor, however, may be absorption via normal lymph vessels.

In the majority of earlier lymphangiographic experiments the contrast medium has been injected deliberately into a tissue, especially into subcutaneous connective tissue or fat (3, 5, 20, 32, 34, 38, 41, 42). The technique has been applied to virtually all kinds of soft tissue, *e. g.* that of muscle (41, 5, 42), lymphatic tissue in lymph nodes or the tonsils (5, 42, 27), lung parenchyma (29, 30), testicular parenchyma (41, 5), and uterus and ovaries (41, 5). Most of these experiments have been performed in animals or on autopsy material but several examinations of human subjects have also been reported, *e. g.* studies of the lymphatics originating from the tonsils (27), in the legs (9), and in malignant tumors of the uterus (33) and breast (17).

The alternative method of introducing the contrast medium into the lymph vessels has been to isolate them surgically and inject the radiopaque substance directly. This method may be applied to large and medium-

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sized lymph trunks. It will be greatly facilitated if a suitable colloidal dye is injected previously near the site of operation, as advised by KINMONTH (22, 23) in 1952. With this technique he studied the lymphatics in patients with idiopathic and postoperative lymphedema (23, 24). Lymphangiography with direct injection of contrast medium into the lymphatics was also performed by MENKES (30) and ZHDANOV (41), in 1932, in experimental animals. CARLSTEN and OLIN in 1951 (8) studied the anatomy of the thoracic duct in cats and its regeneration after surgical trauma; SERVELLE and DEYSSON in 1951 (36) investigated the reflux of intestinal chyle into the lymphatics of the legs in man. A similar technique was adapted by HOGEMAN 1955 (19) in the roentgenographic demonstration of surgically constructed subcutaneous channels in the treatment of lymphedema. WESTHUES (40) in 1935 obtained direct propagation of contrast medium into lymph vessels by lacerating the intestinal mucosa of experimental animals and injecting contrast medium into an occluded part of the intestinal lumen.

The administration of contrast media into serous cavities has been utilized by several investigators. Intraperitoneal injection was used by MENVILLE and ANÉ 1932 (31), CAPUA 1934 (7), EFSKIND 1941 (16), and DURANTEAU et coll. 1955 (15) in various experimental animals. Intrapericardial (2, 6) and intrapleural (6) injections have been made both in experimental animals and in man. The deposition of contrast medium into joints and tendon sheaths has also been reported (41, 42, 30).

Most lymphangiograms have previously been obtained with a more or less modified standard diagnostic roentgen technique and have been at unit scale. For a further survey of earlier work, *vide* BROVELLI and DOLFINI (1936), and CRAMER and KARPATI (1951). In an attempt to widen the radiographic approach to lymph vessel problems, COLLETTE in 1953 applied a microradiographic technique to lymphangiography (10) and obtained excellent high magnification lymphangiograms in experimental animals. The lymph vessels of the rabbit ear were especially suitable for the micro-technique. In studying lymph vessel function, the effects of hyaluronidase on the lymph drainage were observed (9) and, later on, lymph vessel regeneration after resection of lymph nodes in experimental animals was also investigated (11).

In earlier studies, Thorotrast has mainly been used as a contrast medium in experimental animals, but its radioactivity has limited its employment in man. Contrast media of the Diodrast type have chiefly been utilized for the latter, although other contrast media, *e. g.* Angiopac (Union Chimique Belge), which consists of a finely dispersed suspension of contrast oil, have also been tried. The advantage with colloidal contrast media such as Thorotrast, or corpuscular ones such as Angiopac, is that they are not so readily removed as crystaloids (*e. g.* Diodrast) by the

blood circulation from the site of injection. Another advantage is that they do not — in contradistinction to Diodrast — cause local irritation when injected into tissue.

In general investigations of the transformation of the vascular system under various conditions, which are proceeding at our laboratory, we are studying the lymphatic system with a micro-lymphangiographic technique similar to that described by COLLETTE. The results of this work will appear elsewhere; here we shall merely describe our experiences with the micro-lymphangiographic technique itself.

Material and methods

The theoretic calculations and experimental determination of the absorption, etc., in the contrast media described later, were made on the following basis: The mass absorption coefficients for various substances were computed from SIEGBAHN, 1931 (37), or calculated according to JÖNSSON's formula (21). The specific gravities of the contrast media were either determined by standard methods or taken from manufacturer's data. The latter was the case with the chemical composition of the contrast media.

For the measurements of the absorption in the contrast media, frames for absorption cells were prepared from 1 mm thick sheet brass. Two small absorption cells were made close to each other in the same frame, their walls consisting of 40 μ thick cellulose acetate, which was glued to the brass frame. Water was kept in one absorption cell and water + contrast medium in the other. The roentgen absorption in these cells was measured photographic-photometrically from roentgenograms taken at varying kilovoltages on Agfa Printon Rapid Film, this material having been found to possess a linear dose-density curve in the region below unit density. For each absorption cell five to ten separate density determinations were made, using a Zeiss Schnellphotometer. Measurements with both cells filled with water revealed deviations between them of 1 to 3 per cent.

Animals. Thirteen mature rabbits weighing between 2.9 and 3.8 kg were subjected to lymphangiography of the ears or legs. In some cases several experiments were performed in the same animal.

Lymphangiographic technique. Most experiments were performed in living animals. These were anesthetized with Nembutal 20 mg per kg body weight and ether. Freshly killed animals were also utilized.

Thorotrast (Testagar) and Umbradil 35 % (Astra) normally served as contrast media. In a few experiments various concentrations of Micropaque (Damancy) were used.

The contrast medium was injected by hand subcutaneously into an

ear or leg, using a fine (No. 18) needle. Microangiograms were then taken at varying intervals after injection in living or dead animals. In some cases the injected tissue was removed and fixed in a special fixative, which precipitated the contrast medium, and then subjected to routine histologic preparation with embedding in paraffin or beeswax before micro-lymphangiograms were taken. The technique was essentially the same as that in examinations of blood vessels (4).

A Machlett AEG 50 T roentgen therapy tube with tungsten target and 1 mm thick beryllium window served as the source of radiation. It was energized with full-wave rectified D. C. at kilovoltages ranging between 20 and 50. The focus to film distance was varied between 23 and 53 cm. The lymphangiograms were recorded on Agfa Printon Rapid Hochempfindlich Film or Kodak M.R. Plates. The films or plates were wrapped in 12 μ thick aluminium foil and placed in close contact with the tissue examined. Lead plate, 3 mm thick, and lead glass, 10 mm thick, protected the experimenters from exposure. The photographic material was normally developed in Kodak D 19b developer for 2 to 3 minutes, but other developers were occasionally used.

With the technique described, the lymphangiograms were recorded at unit scale. Their definition permitted subsequent enlargement up to 10 to 15 diameters with Agfa Printon Rapid Film and appreciably higher values with Kodak M. R. Plates. The latter type of photographic material was associated, however, with the drawback of appreciably longer exposure times and higher roentgen doses to the tissue; it would therefore seem to be suitable mainly for dead material.

Standard photographic procedures were applied in enlarging the micro-lymphangiograms.

Experimental series

1. Determination of the absorption in contrast media of roentgen beams energized at 20 to 50 kV with the Machlett tube used in the experiments: Varying concentrations of contrast media were utilized, corresponding to 10, 50, and 100 μ thick layers in water. The contrast medium was introduced together with water in one absorption cell; the other cell contained water alone. The absorption in the contrast medium then corresponded to that of a layer of contrast medium within a 1 mm thick tissue, represented by the water.

2. Experimental determination of the qualities of micro-lymphangiograms taken with varying kilovoltages: Micro-lymphangiograms were here taken in rapid succession from the same lymph vessels, using kilovoltages ranging between 20 and 50.

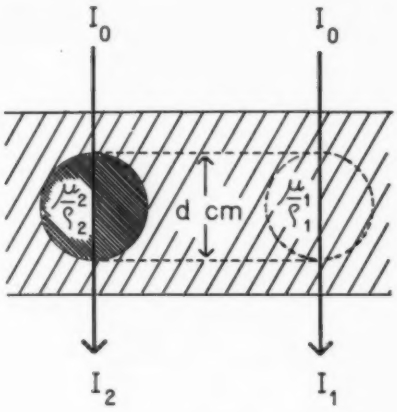

Fig. 1. Schematic representation of absorption of homogeneous roentgen rays in a homogeneous column of contrast medium, having a diameter of d cm (cf. eq. 1—3). The mass absorption coefficients are $\frac{\mu_1}{\varrho_1}$ and $\frac{\mu_2}{\varrho_2}$ respectively, for tissue and contrast medium. The incident roentgen ray intensity is I_0. The transmitted intensities are I_1 for the tissue of the object and I_2 for the column of contrast medium.

3. Study of the propagation of the roentgen contrast media from the site of subcutaneous injection into the lymph vessels, and away from them.

Theoretical aspects of the absorption of roentgen rays in contrast media

The roentgen image of a contrast-filled lymph vessel within a tissue has a contrast (I_1/I_2, cf. Fig. 1) which may be expressed

$$\frac{I_1}{I_2} = e^{d \cdot (\mu_2 - \mu_1)} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where I_1 and I_2 represent transmitted roentgen intensities for the surrounding tissue and for the lymph vessel, e is the basis of the Napierian logarithm, d denotes the thickness of the lymph vessel, and μ_1 and μ_2 the linear absorption coefficients for the tissue and the contrast medium.

The possibilities of influencing the magnitude of the contrast in the roentgen image, for a vessel with a fixed thickness d, naturally lie in changing the linear absorption coefficients for the contrast medium and for the surrounding tissue. In the case of living material, the latter can be changed only by altering the quality of the radiation used. For the contrast medium the linear absorption coefficient may be changed also by altering the chemical composition, in so far as this is biologically practicable.

For an evaluation of the possibilities of obtaining high contrast in the roentgen image by choosing suitable quality of radiation, the absorption in such amounts of Thorotrast and Umbradil 35 % in the roentgen wavelength range which can be applied in micro-lymphangiography will now be discussed.

The linear absorption coefficient μ for a contrast medium is constituted of the properties of the substances contained in it according to the formula

$$\mu = a \cdot \mu_a + b \cdot \mu_b + \ldots + n \cdot \mu_n \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

where a, b, etc. represent the relative amounts of the various substances, and μ_a, μ_b etc. their linear absorption coefficients.

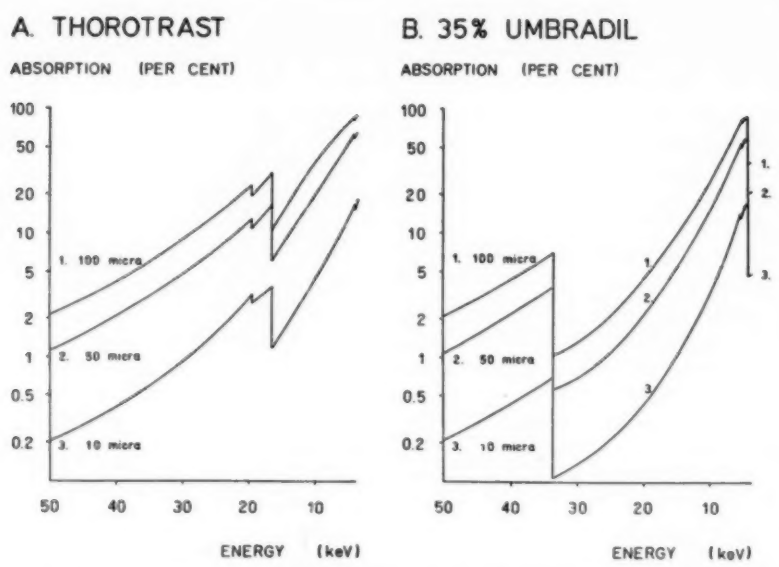

Diagram 1. Theoretically calculated curves for absorption of roentgen rays of various energies in varying layers of Thorotrast and Umbradil 35 %.

The differential linear absorption coefficients (μ_2—μ_1) were calculated for the two contrast media against water, representing soft tissue. The manufacturers' data for the chemical composition were used. The specific gravity of Thorotrast had to be determined and was found to be 1.33 at + 20° C. The average composition of Thorotrast was then calculated at 0.22 g thorium, 1.0 g water, and 0.11 g carbon per cc. For Umbradil 35 % the composition was 0.18 g iodine, 1.0 g water, and 0.11 g carbon; in this calculation a slight approximation was made for carbon, nitrogen, and hydrogen. It is then clear that the factor μ_1, above, representing the surrounding tissue, is eliminated by the amount of water in the contrast medium, provided that the surrounding tissue has a linear absorption coefficient closely resembling that of water. On this assumption, and neglecting the small amounts of carbon in the contrast medium, the equation (1) can be written

$$\frac{I_1}{I_2} = e^{\frac{\mu}{\varrho} \cdot q} = e^{s \cdot \mu} \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

where $\frac{\mu}{\varrho}$ denotes the mass absorption coefficient for thorium or iodine, q the amount of thorium or iodine per square centimeter, s the amount expressed as layer thickness (cm), and μ the linear absorption coefficient for thorium or iodine.

The absorption image in the roentgen beam, expressed in equation (1), is recorded on photographic emulsion, and a micro-lymphangiogram is obtained. For quantitative microphotometric measurements without frames of reference, low densities are sought.

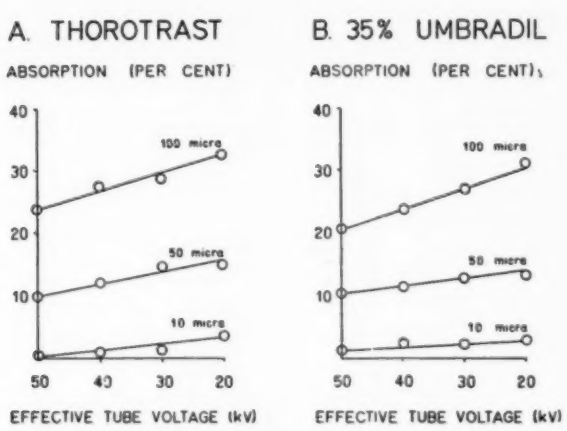

Diagram 2. Experimentally determined curves for absorption of roentgen beams energized at kilovoltages varying between 20 and 50, in different amounts of Thorotrast or Umbradil 35 % per 1 mm water.

For visual inspection, on the other hand — *e. g.* with a magnifying glass or microscope — the aim is to secure the highest density permitted by the source of light employed at inspection, so as to create optimal contrast between the structures studied and their environment.

Micro-lymphangiograms that are to be magnified photographically must have lower densities for good results. We normally expose them below unit density. In this region the photographic emulsion used (Agfa Printon Rapid Film) has a linear dose-density relationship and the incident roentgen ray intensities give proportional densities in the images.

In order to study the requisites for obtaining sufficient contrast in this type of micro-lymphangiogram, the absorption was calculated for varying layers of Thorotrast and Umbradil 35 % in the energy range 5 to 50 keV. In this estimation the absorption coefficients alone were used, the scattering being disregarded. The results of these calculations are shown in Diagram 1. It would seem that even the finest lymph vessels — which are about 10 μ thick — if filled with contrast medium uncontaminated by lymph, would provide a fully sufficient contrast with roentgen rays having energies in the order of 10 to 15 keV.

The above calculations refer, however, to monochromatic roentgen radiation. In most microradiographic work, the broad wavelength spectrum of the total radiation from a roentgen tube is utilized because of the need of a high output, especially in experiments on living material. In this case, calculation of the absorption would necessitate an integration for the whole wavelength range used. In the present study, this integration was simply performed photographic-photometrically in model experiments where the absorption was determined.

Results

The in vitro measurements of the absorption of varying qualities of roentgen rays in varying amounts per square centimeter of Thorotrast and Umbradil 35 % gave the results shown in diagram 2. With 1 per cent (v/v) of the contrast medium (= 10 μ thick layer) the absorption was found to be in the order of magnitude of 0.5 to 2 per cent for both contrast media. These figures are of similar magnitude to the photometric error and the error in thickness of the absorption cells, and are therefore unreliable.

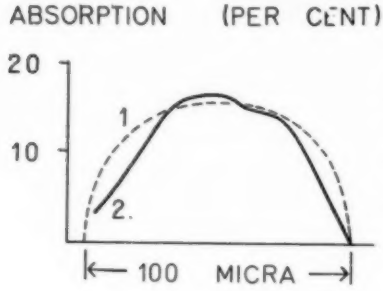

Diagram 3. Absorption curves for 100 μ thick lymph vessel containing Thorotrast. Curve 1 calculated on basis of vessel containing 50 % Thorotrast and 50 % lymph. Curve 2 derived from photometric determination of absorption in 100 μ thick lymph vessel, marked in Fig. 2 a, and assumed to have a circular cross-section. Thickness of the ear was 1 mm. Experimental curve closely resembles calculated curve for equal parts of Thorotrast and lymph.

With 5 and 10 per cent (= 50 and 100 μ thick layers) of the contrast media the absorption was fairly similar for both. The absorption increased with decreasing kilovoltage, but the change was rather small over the investigated range. With 5 per cent of contrast medium the change was from 10 to 13—14 per cent, and with ten per cent solutions the change was from 20—24 to 30—32 per cent for both. This corresponds to an effective wavelength of about 1 Å.

However, the quality of a micro-lymphangiogram is also affected by factors other than the contrast obtained by the absorption in the contrast medium of the roentgen rays. The definition in the image naturally also depends on the geometrical conditions for the image formation and on the granularity of the photographic emulsion. Scattered radiation and photoelectrons may also affect the image and reduce its definition. This factor increases with the energy of the radiation used. Fig. 2 shows two micro-lymphangiograms from a series taken in rapid succession on the same ear, using kilovoltages ranging between 20 and 50, whilst the geometric conditions and the photographic material were the same throughout the experiment. There is a slight difference in contrast and definition between these images, resulting from somewhat lower absorption in the contrast medium at the higher kilovoltage and, presumably, also from an increased disturbing influence of scattered radiation and photoelectrons.

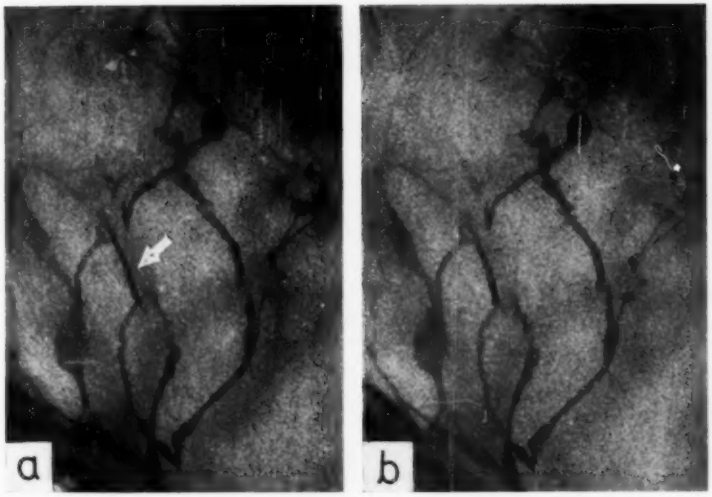

Fig. 2. Micro-lymphangiograms, × 7.5, from a series taken in rapid succession with kilovoltages varying between 20 and 50. For (a) effective kilovoltage was 20 and for (b) 50; the two images differ slightly in quality. The lymph vessels give roentgen images of appreciably varying densities, presumably because of varying proportions of lymph and Thorotrast. Photometric measurements were made on lymph vessel indicated in figure, the results being shown in Diagram 3.

With the technique employed in most experiments on ears, magnifications of 10 to 15 diameters could be obtained. The factor which limited the degree of enlargement of the micro-lymphangiograms was the granularity of the Agfa Printon Film. With special developers, such as Gevaert Nogranol, somewhat finer grain was obtained, but the contrast in the lymphangiograms was then less because of the lower γ value obtained with Nogranol than with the rather hard D 19 b; so here again definition was lost, and longer exposure times were also required. With Kodak M. R. plates developed in D 19 b, the grain permitted about 100 diameters enlargement, but in this case the roentgen dose during the exposure was several hundred times higher. This material therefore could not be used in long-term experiments because of the injurious effects of the radiation on the examined tissue.

In the experiments on the extremities of rabbits it was found that the roentgen dose required was very high with the equipment used, and the definition did not permit appreciable magnification (cf. Fig. 3).

The exposure naturally varied appreciably with the thickness of the tissue examined and also with the technique that was adopted. For rabbit

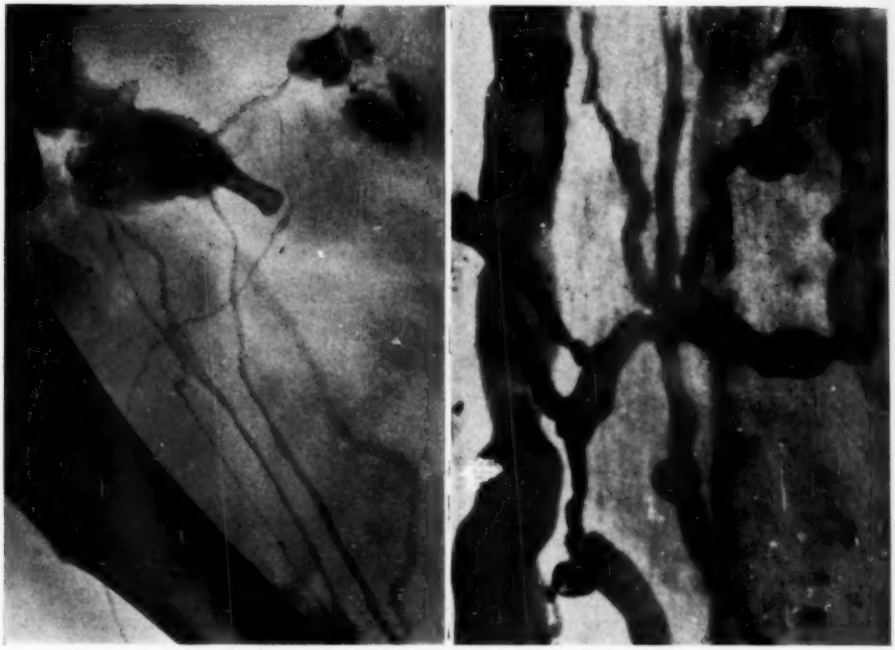

Fig. 3. Fig. 4.

Fig. 3. Micro-lymphangiogram, × 2.5, showing lymph vessels and two lymph nodes in axilla of rabbit injected with Thorotrast in paw.
Fig. 4. Micro-lymphangiogram, × 50, from fixed rabbit ear. Two medium-sized lymph trunks and several small lymph vessels; pearl-string shape of one trunk clearly visible.

ears and with a focus to film distance of 53 cm the exposure varied between 0.6 and 6 seconds for kilovoltages ranging between 50 and 20, when Agfa Printon Rapid Hochempfindlich Film was used.

Behavior of the injected contrast medium. It was found that with Umbradil or Thorotrast, contrast medium could be demonstrated in lymph vessels very shortly after the injection; in fact as soon as a micro-lymphangiogram could be taken, *i. e.* about 10 seconds after the start of the injection. By then, lymph vessels relatively remote from the injection site were already filled with contrast medium. This suggested that the contrast medium had been injected directly into lymph vessels cut by the edge of the needle. This opinion seemed justified when contrast medium containing air bubbles was used and these could be demonstrated in lymph vessels shortly after the injection (Fig. 5).

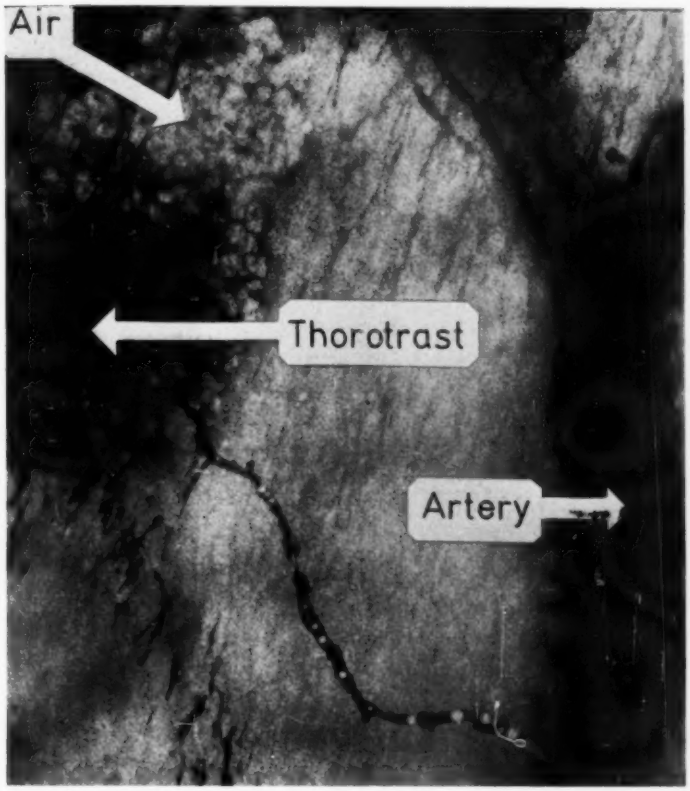

Fig. 5. Micro-lymphangiogram, × 8, from a rabbit ear, showing lymph vessel running from subcutaneous depot of contrast medium to trunks accompanying large arterial branch in middle of ear. Numerous air bubbles in and around contrast depot and also in lymph vessel.

Injections were also made in both the ears and legs of killed animals and lymphangiograms obtained (Figs. 3 and 4).

With a suspension of Micropaque, satisfactory lymphangiograms with very good contrast could sometimes be recorded shortly after the injection, but occasionally we failed entirely to get the contrast medium into the lymphatics. The reason for these failures was not investigated, though it may have lain in the appreciably higher viscosity of the suspensions used, by comparison with the other contrast media. Micropaque was not utilized in further experiments.

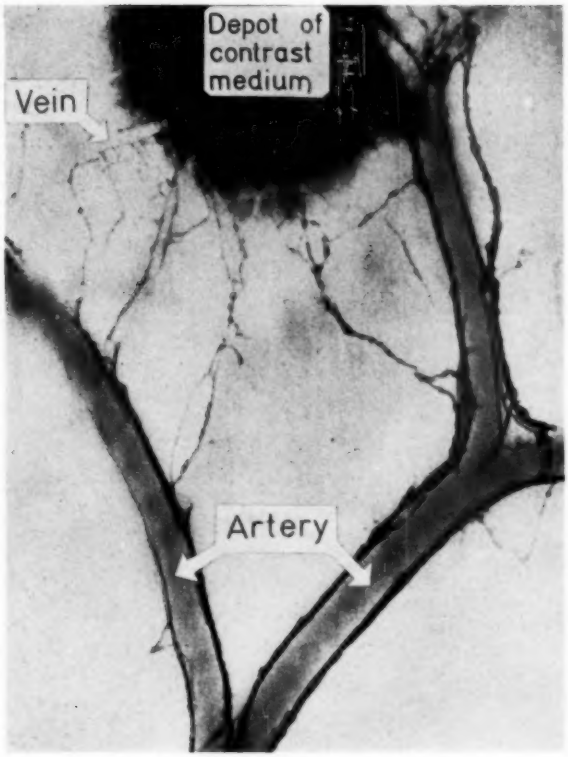

Fig. 6. Micro-lymphangiogram, × 6, from rabbit ear, showing lymph vessels radiating from site of injection to the lymph trunks around large arterial branches.

With Thorotrast, good filling of the lymph vessels was invariably observed in the first micro-lymphangiogram, taken 10 seconds to 3 minutes after its subcutaneous injection. The lymph vessels then appeared more or less unchanged during the first 8 to 9 minutes after the injection of contrast medium; occasionally the filling seemed slightly improved about 3 minutes following it. With the amounts used, the contrast medium gradually left the lymph vessels after the first 8 to 9 minutes, and after 45 minutes it had disappeared. The length of time during which contrast medium remained visible in the lymph vessels depended to a great extent, however, on the amount that was injected subcutaneously. This amount could seldom be estimated very accurately for there was always backflow of contrast medium to the surface through the channel

produced in the tissue by the needle, even if the latter was left in situ after the injection. Hence, experiments involving determination of the time taken for the contrast medium to disappear from the lymph vessels, under varying conditions would seem to be associated with a serious source of error.

Umbradil often gave good initial micro-lymphangiograms but disappeared more rapidly than did Thorotrast; 10 minutes after the injection the lymph vessels no longer contained contrast medium. Occasionally, the first film taken after the injection of contrast medium showed moderate filling of the lymph vessels, and the next one, also taken during the first minutes, an improved filling.

Normally the contrast medium appeared in lymph vessels in a fairly narrow zone between the subcutaneous depot of contrast medium and the abundant lymphatics running along the middle branch of the posterior auricular artery (Figs. 6 and 7). Occasionally, rich lymph-vessel networks were also visualized around smaller arteries and veins (Fig. 8). In the case of injection near the anterior or posterior edge, the lymph flow sometimes followed the margin of the ear. The union of lymph vessel branches could often be distinguished in the films, contrast medium flowing a short distance in a retrograde direction through branches before being stopped by the valves and perhaps also by the lymph flow. The contrast medium never spread over large parts of the ear. By using multiple subcutaneous injections it was possible to obtain filling of a large number of lymph vessels throughout the ear, but it was always evident that a large proportion remained unfilled. This seemed natural because substantial parts of the ear still drained lymph uncontaminated by contrast medium (cf. Fig. 2 and Diagram 3).

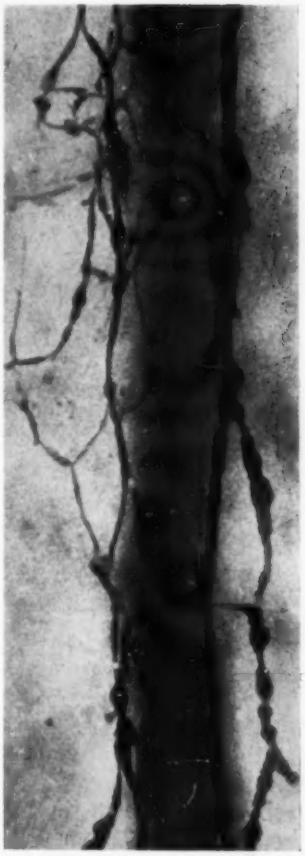

Fig. 7. Micro-lymphangiogram, ×7.5, taken from rabbit ear, shows dense network of lymph vessels and trunks around middle branch of posterior auricular artery. Normally, the medium injected into outer part of ear flows this way.

The subcutaneous depot of contrast medium normally spread concentrically from the site of injection and decreased in density (Fig. 9).

Fig. 8. Micro-lymphangiogram, × 6, from the tissue near tip of rabbit ear. Large number of lymph vessels around arteries and veins visualized in tissue surrounding subcutaneous depot of Thorotrast. Injection needle left in situ but small amount of contrast medium has exuded.

When large amounts were used, the contrast medium was distributed subcutaneously through a great part of the ear, thus darkening the lymph vessels. From 0.01 to 0.05 ml seemed to be the optimal amount for good images of the lymph vessels without darkening of more than a small portion of the ear. With Umbradil the subcutaneous contrast shadow was reduced appreciably in density during the first 15 minutes, but complete disappearance of the contrast medium could not be demonstrated because edema developed and produced a shadow in the region. Thorotrast in no case disappeared completely from the site of injection, but the faint persisting shadow seldom interfered with further lymphangiographic examination of the tissue. No attempts were made to elucidate the state of the subcutaneous tissue from the way in which the contrast medium migrated through it.

When Umbradil 35 % in a dose of 1 ml or more was injected subcutaneously into the ear, necrosis often appeared; with smaller amounts inflammatory reactions were common. In no case were similar effects

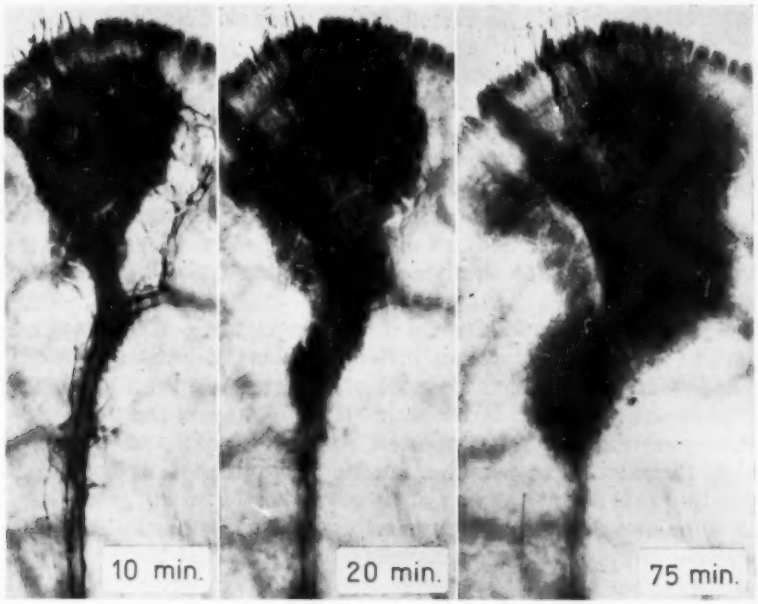

Fig. 9. Micro-lymphangiograms, × 2, taken at varying intervals after subcutaneous injection of Thorotrast into tip of rabbit ear. Contrast depot gradually dispersed over a greater tissue volume and attenuated. The initially good filling of lymph vessels decreases and finally disappears.

observed after the injection of Thorotrast. This is the main reason why we consider Thorotrast to be superior to Umbradil for micro-lymphangiography in animals, in which late radiation injuries are unimportant.

When Thorotrast mixed with hyaluronidase was injected subcutaneously into the rabbit ear (6 experiments), the initial lymphatic spread of the contrast medium was similar to that in the other cases. Nor did the further course differ appreciably in four of the experiments. Here too, it was seen that the time during which contrast medium remained in the lymph vessels was greatly influenced by the amount injected. In two experiments, however, the course differed greatly after the initial stage; the subcutaneous depot of contrast medium spread rapidly through a large part of the ear and was speedily attenuated. Filling of the lymph vessels, which had initially been satisfactory, rapidly decreased and had disappeared after 30 minutes. In these two experiments a contrast shadow gradually appeared in the tissue around the main path of lymph vessels carrying the contrast medium.

Conclusion and comments

The present investigation has shown, in agreement with earlier experience, that lymph vessels fill with contrast media injected subcutaneously. Contrast medium was found to be present in lymph vessels some distance from the injection site after only a few seconds, and this suggested that it had been injected directly into the lymph vessels. The fact that comparatively large particles and minute air bubbles in the injected contrast medium were dispersed in the same way supported this opinion, and so did the observation that the lymph vessels could also be filled in killed animals.

The route of this suppositional direct propagation of contrast medium is not clear, but most probably it is via lacerations produced in the lymph vessels by the injection needle, as suggested by McMaster (28), 1946, in the case of intradermal injections. However, the possibility of a direct communication via leaks in normal lymph vessels cannot be ignored, although this would seem improbable in the light of recent information (18) about the size of these pores and leaks.

In some experiments, the amount of contrast medium present in the lymph vessels appeared to be increased after the first micro-lymphangiograms had been taken. This could have been caused by absorption of contrast medium into the lymph vessels but it is striking that these cases showed none that were not filled by the initial, supposedly mechanical, introduction of contrast medium into the lymphatics.

It seems clear that a mechanical introduction of contrast medium into the lymph vessels occurs with the technique employed and that there is probably also a phase of absorption into those vessels. In our opinion therefore, experiments designed to study the resorption of subcutaneously injected substances such as contrast media, under various conditions, *e. g.* inflammation, or after the administration of drugs such as hyaluronidase, should take into account this probably dual mode of spread into the lymphatics.

The micro-lymphangiographic method applied, utilizing contact microradiography, with the object in close contact with the photographic film or plate, necessitates very soft roentgen rays for the exposure, for otherwise the quality of the images will be too poor for appreciable enlargement. Hence, the objects must necessarily be thin; rabbit ears have proved to be very suitable. In thick objects, the filtration excludes the soft portion of the roentgen beam, and the geometrical conditions are also impaired. With such objects as rabbit extremities the prerequisites for the microtechnique are already greatly reduced. Another effect of the filtration of roentgen beams, containing very soft rays, is the harm done to the tissue by the appreciable radiation doses delivered

during the exposures, which limit the possibilities of long-term experiments.

The main advantage of micro-lymphangiography as compared with other methods, is that repeated images of lymphatics can be recorded with satisfactory magnification in large tissue volumes. With repeated examinations of the same tissue, the method permits of continuous recording of changes in lymph vessel patterns with a precision and clarity that no other method can equal.

As in the case of microangiography on minute blood vessels, however, technical advances may be possible by using projection microradiography, *i. e.* taking microradiograms with the use of a point focus roentgen tube and recording a directly enlarged roentgen image on a photographic film at some distance from the object. This technique, in combination with an electronic image intensifying device, would even make the application of micro-tomography (26) possible. At present, micro-lymphangiography can be applied to small experimental animals; with such a development of the technique it should even be possible to apply it to investigations in man.

SUMMARY

Experiments in micro-lymphangiographic technique were carried out in a number of rabbits, the contrast media being injected into the legs and ears. The latter site was found to be the most suitable. Umbradil 35 % and Thorotrast were employed. It was demonstrated, as previously known, that lymph vessels filled with contrast media injected subcutaneously, and it was concluded that the media were introduced mechanically, probably via lacerations caused by the injection needle.

RÉSUMÉ

Les auteurs ont expérimenté sur un certain nombre de lapins une technique de micro-lymphangiographie, les moyens de contraste étant injectés dans la patte et dans l'oreille. C'est l'oreille qui est le lieu d'injection le plus favorable. L'Umbradil à 35 % et le Thorotrast ont été utilisés. Les auteurs ont montré, comme on le savait déjà, que les vaisseaux lymphatiques sont opacifiés par les moyens de contraste injectés sous la peau et concluent que ces produits y pénètrent mécaniquement, probablement à travers des dilacérations faites par l'aiguille d'injection.

ZUSAMMENFASSUNG

Experimente mit einer mikro-lymphangiographischen Technik sind an einer Reihe von Kaninchen ausgeführt worden; das Kontrastmittel wurde in die Beine oder in die Ohren injiziert. Die letztere Stelle hat sich als die günstigste erwiesen. Umbradil 35 % und Thorotrast wurden benutzt. Es wurde — wie bereits bekannt — demonstriert, dass sich die Lymphgefässe nach subkutan injiziertem Kontrastmittel füllten; es wurde gefolgert, dass die Kontrastmittel mechanisch eingeführt wurden, wahrscheinlich nach Schädigung der Lymphgefässwände durch die Injektionsnadel.

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ROENTGENOGRAPHIC AND TOXICOLOGIC STUDIES ON LEAD EDTA

by

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When considering the composition of a contrast medium for diagnostic roentgenology there are many factors to be taken into consideration, for instance the solubility of the material in physiologic fluids, its toxicity, and its possible hypersensitive reactions.

A roentgen contrast medium should contain an element of as high an atomic number as possible. But taking into account the other factors already mentioned one meets formidable obstacles when trying to find a contrast medium that can be used clinically. Many agents have been tried but only a few have been found suitable. Most of the contrast media used at present contain iodine (atomic number 53, molecular weight 127) or barium (with figures of 56 and 137 respectively) as the contrast-producing substance, the latter mostly in preparations for investigating the alimentary canal. It is well known, however, that neither iodine nor barium are ideal contrast substances, and consequently substitutes are always being sought.

On account of the contrast effect heavy metals such as gold, mercury, lead, bismuth, and thorium should be ideal. Thorium has been used in some preparations of which Thorotrast is the best known. This preparation gives extremely good contrast and does not cause any immediate irritative effect. Its suitability is much restricted, however, because of its radioactivity and its tendency to be retained in the reticuloendothelial system. The other heavy metals are also too toxic to be used in pure form in human subjects in the doses required.

A reasonable attempt to overcome the problem of the toxicity of the heavy metals has been made by binding them to chelating agents. Such agents comprise both organic and inorganic compounds capable

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of forming complexes with metals, especially the alkaline earths and heavy metals. The metal ion is bound in a cyclic or ring structure and is thus made inactive, displaying none of its usual chemical properties. The complex is excreted in the urine and faeces. Ethylenediamine tetra-acetic acid, known as EDTA or Versene, is such a chelating agent. SCHWARZENBACH and FREITAG (1951) have shown that lead forms a complex with EDTA. The disodium salt of the calcium complex of EDTA administered intravenously has been tried with good results as an antidote in lead poisoning.

The idea of using the lead EDTA complex as a roentgen contrast medium was put into practice by SAPEIKA (1954, 1955). He administered lead EDTA to animals in 25 % and 50 % preparations by mouth for roentgenography of the gastro-intestinal tract and by subcutaneous and intravenous injection for urography and for angiography. He considers it "to have many useful features which make it of value in radiographic diagnosis" and "to have advantages over many of the agents at present in use". He also used lead EDTA in human subjects for roentgenography of the oesophagus and of the nasal sinuses as well as for urography.

CLARK and TOMICH (1955), on the other hand, found lead EDTA too toxic to be submitted to clinical trial. They based their conclusions on studies of the excretion of lead EDTA in the urine and faeces in rats and rabbits given various doses of the substance orally and parenterally, and on a histologic examination of the organs of some of the experimental animals. Their series was rather small, however, and consisted of not more than 21 rats and 8 rabbits. Furthermore their experimental period was short, the excretion of lead EDTA being followed up for only two to four days although in most cases the excretion of the complex was still proceeding.

The investigations of CLARK and TOMICH thus stand in need of elaboration. Their paper appeared in October 1955 when the experiments to be described were just nearing completion, and in which both the radio-opacity and the toxicity of lead EDTA were examined.

Material and methods

In 28 experiments about 25 % and 50 % aqueous solutions of lead EDTA, either with or without dextran as added component for obtaining an appropriate viscosity, were used in adult rabbits in doses of 0.2 to 2.7 ml/kg for angiography (arteriography, venography, and lymphography) and for urography.

One-hundred-and-ten albino mice of both sexes were given single doses of $PbNa_2EDTA$ intravenously. The injections were made into a

tail vein. The material was divided into three groups, one group receiving 0.01 ml, one 0.05 ml, and one 0.1 ml per 10 g body weight of aqueous solutions of $PbNa_2EDTA$ with dextran as viscosity regulating factor. Each ml contained 0.517 g $PbNa_2EDTA$ = 0.196 g Pb, and the pH value of the solutions used varied between 7.0 and 7.6. Of the 110 mice, 26 died at different stages of the experimental period. At regular intervals mice from each group were incinerated and the ash polarographically analysed for lead. Most of the lead analyses were made within three months after the administration of the lead EDTA complex. However, a few mice were not killed until about eight months after treatment. In the 0.1-ml group no investigations were made later than 18 days after the administration of the dosage.

A smaller group of 10 mice was given 0.2 ml per 10 g body weight of the same solution. In this group, 7 mice died within five days after treatment. Of the remaining animals 2 were analysed on the 21st day and one on the 262nd day.

The polarographic determinations of lead in whole mice were made as follows.

One mouse was placed in a quartz casserole on a hot plate overnight. The black residue was ashed in an electric oven, and when only a very small amount of carbon was left the ash was heated with a mixture of perchloric and nitric acids until all white fumes had disappeared. After cooling nitric acid was added and the acid evaporated to dryness. The residue was dissolved in a mixture of 50 ml 0.5-M potassium nitrate and 0.1-M nitric acid and, after gelatin had been added, the solution was polarographed between — 0.1 and — 0.8 V according to V. STACKELBERG (1950) and KOLTHOFF and LINGANE (1952).

Blanks were always run. All reagents were free from lead, and the quartz- and glass-ware used was carefully cleaned with concentrated nitric acid.

In a control series of 20 mice no lead could be detected.

Results

Radio-opacity. The solutions of lead EDTA used in these experiments proved to have a very good radio-opacity, and most of the rabbits seemed to stand up quite well to the investigations except for reactions of pain at the time of injection. No such reactions occurred when physiologic saline was injected under the same conditions.

Toxicity. Most of the mice used in the toxicity experiments increased in weight during the experimental period.

No ill-effects were observed at the site of injection except in the group injected with 0.2 ml per 10 g body weight of the solution. This group is

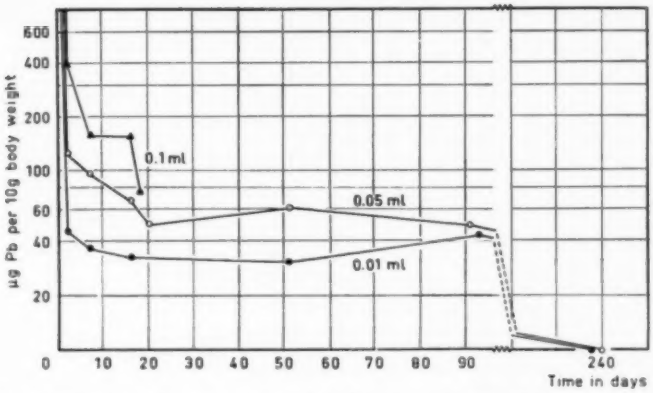

Diagram 1. Retention of lead in mice treated intravenously with three different doses of solutions of lead EDTA containing 0.517 g $PbNa_2EDTA$ = 0.196 g Pb per ml.

not included in Diagram 1. Most of these 10 mice showed circulatory disturbances in the tail, gangrene developing at the tip. Two animals of this group were killed and analysed for lead 21 days after injection, the lead values being 200 and 146 µg per 10 g body weight respectively. The third mouse, killed 262 days after treatment, was free from lead.

From the toxicity experiments, the results of which are shown graphically in Diagram 1, it may be concluded that after intravenous administration of lead EDTA most of it is excreted very rapidly but that some of the metal is deposited in the body. To begin with, the amount of the retained lead is greater the larger the injected dose. From the first two days to about three weeks after treatment the deposit of lead successively diminishes, but after three weeks it remains constant for many months. Whether or not the value of the lead retained during this period is independent of the dose injected remains to be studied in a larger series. It will be noted that some time between three and eight months after injection all lead disappears from the body.

Discussion

As could be expected from the atomic number of lead the radiographic experiments proved lead EDTA to have very good radio-opacity. The toxicity experiments showed, however, that in the living body the elimination of lead after administration as lead EDTA is too slow and unsatisfactory to allow the substance to be used as a roentgen contrast medium in clinical practice.

The results of the toxicity experiments may be explained by the dissociation of the lead EDTA complex: it may be deduced that in the living body the complex is broken down to yield free lead ions. The stability of the lead EDTA complex is dependent on several factors, chiefly pH, but the presence of competing ions is also of considerable importance.

The effect of pH on the dissociation may be calculated as follows.

The four dissociation constants of EDTA, shortly written H_4Y, have the following values (SCHWARZENBACH and ACKERMANN 1947): $pK_1 = 2.00$; $pK_2 = 2.67$; $pK_3 = 6.16$; $pK_4 = 10.26$.

The complex constant of lead EDTA is $K = 10^{18.2}$ (SCHWARZENBACH and FREITAG 1951).

From these figures it is possible to calculate the amount of free lead ions at different pH.

If the concentration of the lead complex is C,

$$\text{then } [Pb^{2+}] + [PbY^{2-}] = C \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 1,$$

$$\text{and } [H_4Y] + [H_3Y^-] + [H_2Y^{2-}] + [HY^{3-}] + [Y^{4-}] + [PbY^{2-}] = C \quad \ldots\ldots\ldots\ldots \quad 2.$$

Further, from definition,

$$\frac{[H^+]\,[H_3Y^-]}{[H_4Y]} = K_1 = 10^{-2.00} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 3,$$

$$\frac{[H^+]\,[H_2Y^{2-}]}{[H_3Y^-]} = K_2 = 10^{-2.67} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 4,$$

$$\frac{[H^+]\,[HY^{3-}]}{[H_2Y^{2}\ ]} = K_3 = 10^{-6.16} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 5,$$

$$\frac{[H^+]\,[Y^{4-}]}{[HY^{3-}]} = K_4 = 10^{-10.26} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 6,$$

$$\frac{[PbY^{2-}]}{[Pb^{2+}]\,[Y^{4-}]} = K = 10^{18.2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 7.$$

From these equations we get

$$\frac{A\,(C - [Pb^{2+}])}{[Pb^{2+}]^2} = K \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 8,$$

where $$A = \frac{[H^+]}{K_4} + \frac{[H^+]^2}{K_3K_4} + \frac{[H^+]^3}{K_2K_3K_4} + \frac{[H^+]^4}{K_1K_2K_3K_4} + 1.$$

But as $[Pb^{2+}]$ is very small compared with C, equation 8 may be written

$$\frac{A \cdot C}{[Pb^{2+}]^2} = K \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 9,$$

$$\text{or } [Pb^{2+}] = \sqrt{\frac{AC}{K}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad 10.$$

In Diagram 2 the relationship between pH and $[Pb^{2+}]$ based on Equation 10 is shown for two different values of C, *e. g.* 1-M and 0.01-M. In practice these two values can be considered as extremes.

At a pH lower than 4, Equation 9 and consequently also 10 are not valid. The dissociation of the complex is then higher than calculated from the equation.

The competing ions may be divided into two groups, those competing *with* EDTA by their tendency to combine with lead, and those which compete *for* EDTA. This is of special significance for such a complex biologic system as the living organism. As an example of the former group the chloride ion may be mentioned. If lead ions are set free from the lead EDTA complex, Pb combines with Cl to form $PbCl_2$ and higher complexes, further dissociation of lead EDTA being the consequence. In the stomach, for instance, there must be considerable dissociation of lead EDTA, partly because of the low pH and partly as a consequence of the free chloride ions present.

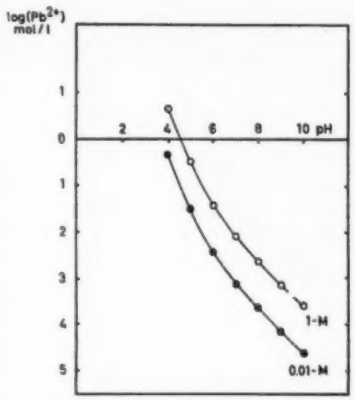

Diagram 2. Relation between free lead ions, dissociated from the lead EDTA complex, and pH at two different concentrations of the complex, 1-M and 0.01-M. Graph calculated from Equation 10.

The metals that compete for EDTA form stable complexes with the chelating agent with a strength comparable to that of lead. Thus the presence in the body of such metals as iron and copper and even calcium favours the dissociation of the lead EDTA complex.

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SUMMARY

The radio-opacity and toxicity of lead EDTA were examined. In angiography and urography in rabbits lead EDTA 25 % and 50 % proved to give very good radio-opacity, but to be too toxic to be submitted to clinical practice. Polarographic analysis of the ash of killed and incinerated mice given various doses of lead EDTA intravenously revealed that lead was retained in the body for many months, the retention being due to dissociation of the lead EDTA complex. The influence of pH and competing ions on the dissociation of the complex is discussed.

ZUSAMMENFASSUNG

Die radiologische Opazität und die Toxizität des Blei EDTA wurden untersucht. Bei der Angiographie und Urographie von Kaninchen ergab Blei EDTA in 25 %-iger und 50 %-iger Lösung sehr gute Kontraste, war jedoch allzu giftig, um zur klinischen Anwendung zugelassen zu werden. Die polarographische Analyse der Asche getöteter und eingeäscherter Mäuse, denen Blei EDTA in verschiedenen Dosen intravenös gegeben worden war, zeigte, dass Blei mehrere Monate lang im Körper retiniert wurde; die Retention war durch die Auflösung des Blei EDTA-Komplexes bedingt. Der Einfluss des pH und der konkurrierenden Ione auf die Dissoziation des Komplexes wird beschrieben.

RÉSUMÉ

L'auteur a étudié l'opacité radiologique et la toxicité du sel de plomb de l'EDTA. Utilisé sur des lapins en angiographie et en urographie, le sel de plomb de l'EDTA à 25 % et 50 % a fourni une très bonne opacité radiologique, mais s'est montré trop toxique pour être employé en clinique. L'analyse polarographique des cendres de souris tuées et incinérées ayant reçu des doses variables de sel de plomb de l'EDTA par voie intraveineuse a montré que le plomb reste fixé dans le corps pendant plusieurs mois, cette rétention étant due à la dissociation du composé EDTA-plomb. L'auteur examine l'influence du pH et des ions en compétition sur la dissociation de ce composé.

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PROTON MAGNETIC RESONANCE OF HUMAN CERVICAL MUCUS DURING THE MENSTRUAL CYCLE

by

Erik Odeblad and *Ulla Bryhn*

Cyclic changes in the human cervical mucus were observed as early as the middle of the 19th century and have in the last two decades been the subject of extensive investigations. Among other matters studied have been the macroscopic and general appearances (SEGUY and VIMEUX 1933) and the crystallization pattern (*e. g.* by PAPANICOLAOU 1945, 1946, by RYDBERG 1948, and by ZONDEK 1954). The amount of dry substance (BERGMAN 1950), the viscosity (LAMAR, SHETTLES and DELFS 1940), 'flow-elasticity' and 'Spinnfähigkeit' (CLIFT 1945), and the amount of reducing substance (VIERGIVER and POMMERENKE 1946) have also been investigated. The studies have mainly been undertaken in order to correlate changes in the properties of the mucus with the time of ovulation, these being of considerable practical importance, especially for timing the optimal day of conception in cases of reduced fertility. In addition, changes in the cervical mucus are of considerable interest from theoretic viewpoints. In the present study we briefly report some preliminary observations on the proton magnetic resonance spectra of the human cervical secretion in various phases of the menstrual cycle.

Principles of nuclear magnetic resonance. Proton magnetic resonance spectroscopy is specific for the hydrogen nuclei in any chemical or physical state. The resonance or absorption line occurs in the radiofrequency part of the electromagnetic spectrum when a sample containing hydrogen nuclei is placed in a magnetic field of several thousand gauss; it is due to the elementary process of absorption of a low-energy electromagnetic quantum when a proton spin flips from a lower to a higher energy orien-

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tation in the bulk magnetic field. The total ensemble of proton spins may return back to their original distribution of orientations by the process of 'spin-lattice relaxation'.

The ideal shape of a resonance spectrum, or signal, will be a single, very sharp peak or line. In gaseous, liquid, and solid matter minor perturbations of different kinds of the proton resonance signal occur. These perturbations reflect the chemical and physical environments of the hydrogen nuclei and are therefore of great importance in studying the chemical and physical state of the sample. Signal size, signal width, and signal position, may be affected by these perturbations.

An introductory presentation of these problems is given in a review of nuclear magnetic resonance in biology and medicine (ODEBLAD 1956). The excellent book by ANDREW (1955) contains the physical essentials of nuclear magnetic resonance and is referred to for more detailed information.

Clinical material. About three hundred women employees were subjected to routine gynecologic examination and specimens taken from a number. The samples investigated fulfilled the following criteria: 1) The general and local condition of the patient appeared to be perfectly normal on examination. 2) Homogenous cervical mucus, which could be removed easily by suction and essentially without any mechanical trauma or irritation of the cervix was present. 3) No contamination of the specimens from blood or vaginal contents was permitted. Some women were subjected to repeated collecting of mucus. Most samples were concomitantly examined for the amount of dry substance and crystallization pattern, and vaginal smears were also collected. A satisfactory phase determination could be obtained by comparing menstrual data, the amount of dry substance in the mucus, the crystallization pattern and the vaginal smears as well as the basal body temperature. A total of 24 examined specimens form the basis of the present report.

Magnetic resonance technique. Samples of about 10 to 30 mg of human cervial mucus were introduced in small thin-wall test tubes and placed in the radiofrequency transmitter coil of the spectrometer, described in detail by LINDSTRÖM and BHAR (1956). During the recording, the sample was rotated at a speed of 15 to 60 c/s. The magnetic field was 3,825 gauss, the radiofrequency 12.3 MC/sec, and the sweep-rate of the field through the resonance condition about 4 milligauss/sec (or about 1 ppm/sec). The resolution was about 0.3 ppm (ppm = parts per million).

Results. Some typical magnetic resonance signals are shown in Fig. 1. As indicated, the postmenstrual signal consists mainly of a single line of a width of about 1 ppm. As the cyclic phase approached midcycle, this narrow peak decreased in size and a new, usually broad, component

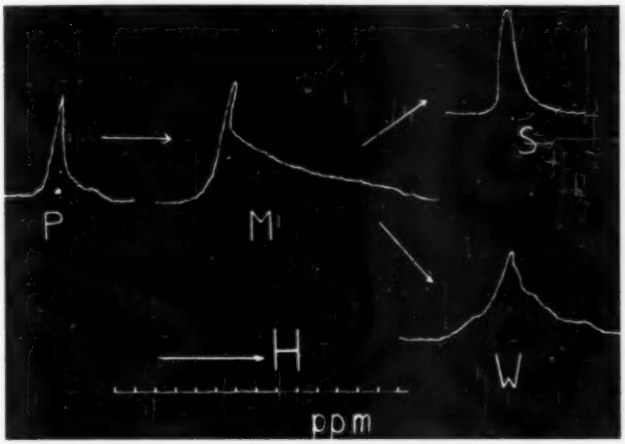

Fig. 1. Typical proton magnetic resonance signals of human cervical secretion. P = postmenstrual signal, M = midcycle signal, S = signal in secretory phase and W = signal in late phase of menstrual cycle without signs of corpus luteum-function. Abscissa: Scale in ppm. Ordinates (not comparable): Signal amplitude. H = direction of bulk magnetic field.

slightly displaced towards a higher field occurred. At midcycle, nearly the whole spectrum consisted of this broad peak, which then appeared to be displaced about 5 ppm from the narrow component and to have half-width of about 3 ppm. The narrow peak was now detected only with difficulty. The total area of the resonance signal was probably considerably larger at midcycle than in the beginning of the cycle though this observation was somewhat uncertain owing to the indefinite reproducability of the signal amplification and variations in the amount or in the coil-filling factor of the cervical sample under study. After midcycle was passed the proton magnetic resonance signal seemed to depend upon whether any luteal activity had occurred or not. If signs of an active corpus luteum were present (diphasic temperature curve, disappearance of arborization, increased dry substance in the cervical mucus, or cytologic evidence) the signal appeared to return more or less to the early postmenstrual pattern. In cases in which it was suspected that no formation of corpus luteum had taken place the signal contained a broad, non-displaced component, or was similar to a signal shortly before midcycle was reached. The fraction of total magnetic resonance signal area occupied by the broad component during the secretory cycle is shown schematically in Diagram 1.

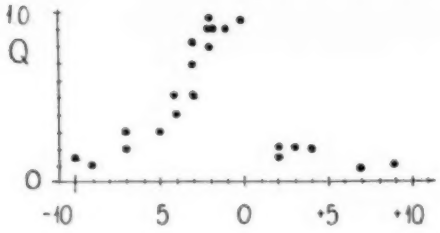

Diagram 1. Variation of Q (= ratio of broad component to total signal area) in the menstrual cycle. Cycles normalized to midcycle (presumed day of ovulation = 0).

Discussion

The present experiments indicate that extensive changes in the proton magnetic resonance signals occur in the human cervical mucus during the normal menstrual cycle. It seems reasonable to believe that increased stimulation of the cervical glands with oestrogens gives rise to the change in the resonance signal at midcycle as well as with other physio-chemical alterations occurring at that time (see references given in the introduction). The return to the postmenstrual pattern in the normal secretory phase is suspected to be due to the additional effect of progesterone on the cervical glands, since it has been shown by PALMER (1941, 1944), ABARBANEL (1946), and ZONDEK (1954), that progesterone in an appropriate concentration inhibits most of the other typical changes in the cervical secretion brought about by oestrogens. The shape of the resonance signal in cases of probable deficient corpus luteum function support this view.

It is also of great importance to try to interpret the observed signals as far as possible physically. An attempt at interpretation on the basis of the present report and some additional observations will be presented in a forthcoming paper.

Finally it may be stated that the present investigation using proton magnetic resonance spectroscopy for cervical mucus has revealed some previously unknown findings connected with the physico-chemical structure of the mucus and disclosed a property subjected to normal cyclic variations. These findings have necessitated extended investigations which are currently being performed. Due to the simplicity of the method, provided that nuclear magnetic resonance equipment is available, the findings may also be of practical value in the future for estimating the phase of the genital cycle as reflected in the cervical function.

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SUMMARY

Changes in the properties of the cervical mucus in relation to the time of ovulation are of practical and theoretic interest and prompted the present investigation. Preliminary observations on the proton magnetic resonance spectra of the cervical secretion in various phases of the menstrual cycle are presented.

ZUSAMMENFASSUNG

Veränderungen der Eigenschaften des Vaginalschleimes in Beziehung zur Ovulationszeit sind von praktischem und theoretischem Interesse und haben zu der vorliegenden Studie stimuliert. Präliminäre Beobachtungen an protonmagnetischen Resonanzspektren des Cervixsekretes in verschiedenen Phasen des Menstruationszyklus werden vorgelegt.

RÉSUMÉ

Les modifications des propriétés du mucus cervical en fonction de la date de l'ovulation ont un intérêt pratique et théorique et ont incité à faire les présentes recherches. Les auteurs présentent des remarques préliminaires sur les spectres de résonance magnétique des protons de la sécrétion cervicale aux diverses phases du cycle menstruel.

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COMPARATIVE BIOLOGIC EFFECTS OF 30 MeV_p AND 220 kV_p ROENTGEN RAYS AND 0.4 MeV GAMMA RAYS AT 8—9° C

by

K. C. Bora

It was reported previously (Bora 1955) that at the dosage level of 100 to 600 r and radiation intensities of 8 r and 15 r per minute, pulsed and filtered 30 MeV_p roentgen rays (from the Synchrotron of the Department of Radiotherapeutics, Cambridge University, England) and 0.4 MeV gamma rays from radio-iridium Ir^{192} produced equal frequencies of chromosomal aberrations (and 220 kV_p roentgen rays about 1.4 times more than those produced by either of them) in the microspores of *Tradescantia bracteata, clones* 20^2 and 20^3, irradiated at 25° C and kept at the same temperature until the time of fixation. It was also reported that 400 r of 30 MeV_p roentgen rays produced anomalously low frequencies of chromosomal aberrations as compared to 300 r of the same radiation. It was found difficult to understand why the particular dose of 400 r should show anomalous results in two successive experiments.

The experiments now to be described were designed firstly to find out relative biologic efficiencies of the same radiations at 8 to 9° C and to investigate if they produce any differential effect on the mitotic speed; and secondly to gather more information as regards the anomalous effects of 400 r of 30 MeV_p roentgen rays.

Material and method. Shoots of *Tradescantia bracteata, clone* 20^2, were collected about 24 hours prior to irradiation and kept at 10° C in a control chamber until the time of irradiation at 8 to 9° C. They were transferred to a control chamber at 24° C ± 1 about 20 minutes after irradiation and remained there until the time of fixation. The cold treat-

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ment previous to irradiation was planned to give the microspores an initially uniform mitotic speed after irradiation. By this means any differential effect of the radiations on the mitotic speed would be revealed by the output and proportions of aberrations examined at different mitotic phases after irradiation. Fixations were made 72 and 137 hours after irradiation. A thermos bottle with a suitable device fixed to the cork to hold the plants 4.7 cm away from the lower surface of the latter was used for keeping the plants immersed in icecooled water at the time of irradiation. The rise of temperature during irradiation was less than 1° C. The minimum dosage rate obtained from the Synchrotron was 4.9 r per minute at a distance of 83.7 cm from the target; 4.9 r and 5.05 r were the dosage rates obtained from the 220 kV_p roentgen machine and radio-iridium Ir^{192} respectively.

As regards the second aim of the investigation the control measures and the time of fixation were similar to those of previous experiments (Bora 1955). Owing to certain technical difficulties it was not possible to obtain either of the dosage rates used previously. The maximum output outside the collimator was 5.4 r per minute. In order to examine whether the time sequence of giving 400 r during the treatment had any effect on the aberration yields, the two doses of 400 r, shown as 400 r, I and 400 r, II, were separated by two successive doses of 500 r and 300 r.

Table 1

Dose 500 r, dosage rate about 5 r per minute, temperature 8 to 9° C, fixation time 72 hours

Type of radiation	Energy	No. of microspores		Chromosomal aberrations per 100 microspores					
		Total	% damage	Chromosome reunions	Simple chromosome breaks	Chromatid breaks	Minutes	Total chromosome breaks	Simple chromosome breaks & minutes
Roentgen	220 kV_p	385	80.5	72.98	35.58	4.15	45.97	181.55	81.55
Roentgen	30 MeV_p	519	62.23	41.23	21.57	4.81	29.67	104.04	51.25
Gamma	0.4 MeV	390	84.61	81.02	29.23	4.87	64.10	191.28	93.33

Experimental data. From the results summarised in Table 1, it will be noted that whereas the frequencies of aberrations produced by 220 kV_p roentgen rays and 0.4 MeV gamma rays are about equal, those of 30 MeV_p roentgen rays are comparable to previous findings. The data presented in Table 2 are remarkable for two reasons; firstly,

Table 2

Dose 500 r, dosage rate about 5 r per minute, temperature 8 to 9° C, fixation time 137 hours

Type of radiation	Energy	No. of microspores		Chromosomal aberrations per 100 microspores					
		Total	% damage	Chromosome reunions	Simple chromosome breaks	Chromatid breaks	Minutes	Total chromosome breaks	Simple chromosome breaks & minutes
Roentgen	220 kV_p	375	79.2	74.13	27.20	2.01	41.6	175.46	68.88
Roentgen	30 MeV_p	125	77.60	62.60	39.20	1.04	50.04	164.00	89.60
Gamma rays	0.4 MeV	375	95.20	105.33	116.00	1.86	140.8	326.66	256.88

the gamma rays have consistently produced significantly more chromosome aberrations than either 220 kV_p or 30 MeV_p roentgen rays; secondly, the proportion of simple chromosome breaks produced by gamma rays is about four times higher than those by 220 kV_p roentgen rays. Only one slide was available for the shoots receiving 30 MeV_p roentgen rays. Although it is unwise to rely on the evidence from a small sample a comparison shows that, on the whole, the frequencies are not significantly different from those of 220 kV_p roentgen rays.

Table 3

Doses 300, 400 and 500 r, intensity 5.4 r per minute, temperature 24.5 ± 0.5° C, time of fixation 72 hours

Doses	No. of microspores		Chromosomal aberrations per 100 microspores					
	Total	% damaged	Chromosome reunions	Simple chromosome breaks	Chromatid breaks	Minutes	Total chromosome breaks	Simple chromosome breaks & minutes
500 r	365	51.23	27.94	14.79	6.84	16.43	70.68	31.22
400 r I	581	48.36	26.16	14.80	9.50	22.89	67.12	37.69
400 r II	410	46.09	20.24	19.26	9.02	16.55	59.75	35.81
300 r	274	32.11	13.50	10.94	5.83	6.20	37.95	17.14

Table 3 shows that chromosomal effects of 400 r of 30 MeV_p roentgen rays are the same whether the dose is delivered at the beginning or end of the experiment. In both cases the overall effects of 400 r are significantly greater than those of 300 r. One may be inclined to consider that any anomaly recorded in the previous experiments could perhaps be attributed to sampling errors. But it should be pointed out that since dosage rate is an important factor in radiobiologic experiments of this type and full details about the breakage mechanism of chromosome is yet to be known, these experiments may not be strictly comparable.

Discussion

It is generally agreed that there is a close correlation between relative biologic efficiency of radiations and specific ion densities. That such may be the case was shown by previous experiments at 25° C. It is almost certain that these values are not absolute but vary according to the biologic criteria studied and factors controlling the metabolic processes disturbed by radiation. It must be emphasized that the mechanism of chromosome breakage, about which very little is known at present, is a complicated problem and the frequencies of chromosomal aberrations are controlled by internal as well as external factors. A correct estimate of the rbe will be obtained only when the differential actions of radiations on the metabolic processes are known. Since the radiosensitivity of the chromosome is not the same throughout the whole mitotic cycle, prophase to prophase, any appreciable effect of radiation on the speed of mitosis will result in alteration in the frequencies of chromosomal

aberrations. Chromosomes, irradiated at the resting stage alone, are not a favourable material for such studies but they could be considered a good material for obtaining standard values of rbe for comparing with those at other stages and also for studies on the effects of radiations on the mitotic speed.

Qualitative differences of biologic effects produced by radiations have never been thoroughly investigated. Most of the data so far obtained deal with quantitative measurements. Since the basic forces supposed to be responsible for the production of biologic effects are believed to be the same for all ionizing radiations, it may not seem possible that a radiation whether sparsely or densely ionizing should produce effects qualitatively different for each radiation.

The results of Table 1 show that a qualitative difference may exist between gamma and roentgen rays of energies employed in these experiments. The frequencies of aberrations produced by gamma rays are much more than the expected values. Even if one accepts the upper limit of 10 % calibration error, the output is too large as compared to previous results. Whether it is due to primary or secondary action of the gamma rays is difficult to visualise at present, but it would be reasonable to suppose that somewhat different mechanisms are involved in the induction of chromosome breaks by roentgen and gamma rays.

Table 4

Type of radiation	Fixation time in hours	Ratios			
		Simple chromosome breaks/ Total chromosome reunions	Simple chromosome breaks and minutes/ Total chromosome reunions	Simple chromosome breaks/ minutes	Total chromosome breaks/ Total chromosome reunions
220 kV_p roentgen rays	72	0.48	1.12	0.77	2.48
	137	0.37	0.92	0.65	2.37
Ir^{192} 0.4 MeV gamma rays	72	0.36	1.15	0.46	2.36
	137	1.10	2.43	0.82	3.10
30 MeV_p roentgen rays	72	0.52	1.24	0.72	2.52
	137	0.63	1.44	0.78	2.63

The proportions of aberration types can be taken as a measure of radiosensitivity and the physical state of the chromosomes at the time of irradiation. Ratios obtained by dividing simple chromosome breaks, exchange breaks and minutes by the total number of reunions are presented in Table 4. It is of interest to note that all the ratios belonging to a particular category and treatment, except those of gamma rays, fixation time 137 hours, are comparable to one another and suggest a uniform radiosensitivity throughout the period from 72 hours to 137 hours

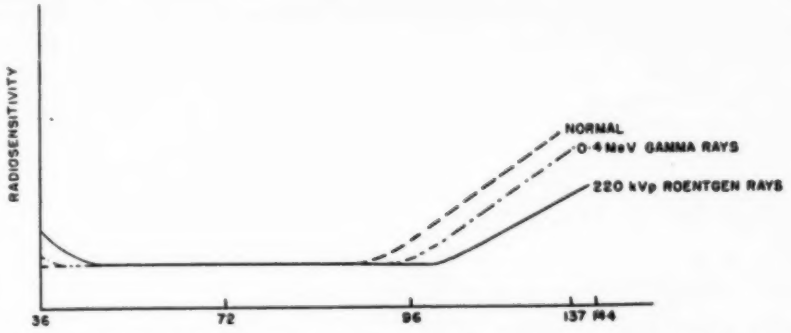

Diagram 1. Relationship between radiosensitivity and radiation energy. Time in hours.

after irradiation. The exceptionally high ratios shown by microspores treated with gamma rays and fixed 137 hours after irradiation may at once suggest that a different type radiation action has taken place in this case. In this connection two assumptions are worthy of consideration: 1) the mechanism of chromosome breakage by roentgen and gamma rays may be dissimilar at different mitotic stages, depending on chemical and physical nature of the chromosomes, 2) the primary actions of radiations are similar but a differential action exists in relation to secondary actions, for example, effect on the mitotic speed. Diagram 1 shows the proposed relationship between radiosensitivity and differential radiation effects on the mitotic speed. The scale and the lines drawn are arbitrary; they represent only the probable pattern of relationship that may exist between mitotic speed and radiation quality. The first assumption demands more information on the chemical and physical nature of the resting stage chromosomes during the developmental phases. Since useful information about these points is still lacking, it will not be worthwhile to judge the probable merits of this assumption at present. The second assumption provides ample scope for fitting the experimental data within its framework. According to it, the increased yield of chromosome aberrations shown by gamma rays may not be due to the primary differential effects but due to the less effectiveness of those rays in slowing down the mitotic speed; 220 kV_p roentgen rays, on the other hand, being more effective, delay the appearance of more radiosensitive chromosomes at the time of examination and therefore show a screening effect. On this assumption the value of rbe shown by irradiations on the types of effect discussed here can never be absolute. The differential effect of radiations as revealed by these experiments is of no important consequence from the therapeutic and genetic points of view due to the fact that the overall effect is not altered either in quality or quantity;

it simply appears earlier in one case and later in the other. It, however, points to the fact that the biologic evaluation of radiations is a problem which requires comprehensive knowledge of the effects of radiations on the biosynthetic processes.

Acknowledgment

I wish to express my gratitude to Prof. J. S. MITCHELL, for his continued interest in the problem. My thanks are due to Miss R. D. SAUNDERS for technical assistance.

SUMMARY

Experiments on the effects 30 MeV_p^- and 220 kV_p^+ roentgen rays, and 0.4 MeV gamma rays on the production of chromosomal aberrations in the microspores of *Tradescantia bracteata* at 8 to 9° C show that a qualitative difference in biologic actions exists between roentgen rays and gamma rays. For the same dose and intensity 0.4 MeV gamma rays appear to be less effective in slowing down the mitotic speed, *i. e.* the biochemical synthesis of chromosomes, than 220 kV_p roentgen rays.

ZUSAMMENFASSUNG

Experimente über die Einwirkung von 30 MeV_+ und 220 kV_+ Röntgenstrahlen sowie 0.4 MeV Gammastrahlen auf die Erzeugung von Chromosomenabweichungen der Mikrosporen von *Tradescantia bracteata* bei 8—9° zeigen, dass ein qualitativer Unterschied in der biologischen Wirkung zwischen Röntgenstrahlen und Gammastrahlen besteht. Für gleiche Dosis und Intensität scheinen die 0.4 MeV Gammastrahlen bezüglich der Verlangsamung der Mitosengeschwindigkeit, d. h. der biochemischen Synthese der Chromosomen, weniger wirksam zu sein als die 200 kV_+ Röntgenstrahlen.

RÉSUMÉ

Des expériences sur les effets des rayons roentgen de 30 MeV_p et de 220 kV_p et des rayons gamma de 0.4 MeV sur la production d'aberrations chromosomiques dans les microspores de *Tradescantia bracteata* à 8—9° montrent qu'il y a une différence qualitative d'actions biologiques entre les rayons roentgen et les rayons gamma. Pour la même dose et la même intensité, les rayons gamma de 0.4 MeV se montrent moins capables de ralentir la vitesse de mitose, c'est-à-dire la synthèse biochimique des chromosomes, que les rayons roentgen de 220 kV_p.

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AUS DEM PRIVATEN RÖNTGENINSTITUT VON DR AP. YIANNAKOPOULOS, A. O. PROF. AN DER NATIONALEN UNIVERSITÄT, ATHEN, GRIECHENLAND.

ÜBER DIE UNMÖGLICHKEIT EINER SCHICHTDARSTELLUNG PATHOLOGISCHER VERÄNDERUNGEN ANHAND GEOMETRISCHER UNTERSUCHUNGEN

von

Ap. Yiannakopoulos

Es ist bekannt, dass die gewöhnliche Schichtbilduntersuchung nur unvollkommenen Aussagewert über Veränderungen in einer Schicht hat, weil durch darüber- oder darunterliegende stärker strahlenabsorbierende Gewebe Verwischungsschatten entstehen können, die eine Differenzierung des Schichtbildes unmöglich machen. Darüberhinaus darf jedoch nicht vergessen werden, dass die Schichtdarstellung eines Objektes allein deshalb nicht möglich sein kann, weil darüber- oder darunterliegende strahlenabsorbierende Körper eine Freiprojektion unter den angewandten Bedingungen (Länge der Fokusbahn, Abstand zwischen Fokus und Film u. a.), absolut nicht zulassen. In dieser Hinsicht fanden bisher vor allem das Knochengewebe und die grossen Gefässe, wenn auch ohne theoretische Untersuchungen, Beachtung. Die Projektionsverhältnisse von zwei Objekten, etwa zweier pathologischer Veränderungen innerhalb eines homogenen Gewebes (z. B. Lunge), wurden jedoch bisher noch nicht eingehend geometrisch untersucht. Die vorliegende Arbeit hat sich deshalb zur Aufgabe gemacht, mit rein geometrischen Methoden die Grenzen einer Projektionsmöglichkeit von in einer Schnittebene liegenden Objekten anzuzeigen, wenn darüber oder darunter gänzlich strahlenabsorbierende Objekte liegen. Dabei wurde die Fokusbahn stets geradlinig in einer Richtung verlaufend angenommen.

Fall A. In Diagramm 1 sei in der Schnittebene ein schattengebender Körper K_1 (Durchmesser $d_1 = 2\ r_1$) durch seine kreisförmige Schnittfläche dargestellt. Ein zweiter

Bei der Redaktion am 3. Oktober 1956 eingegangen,

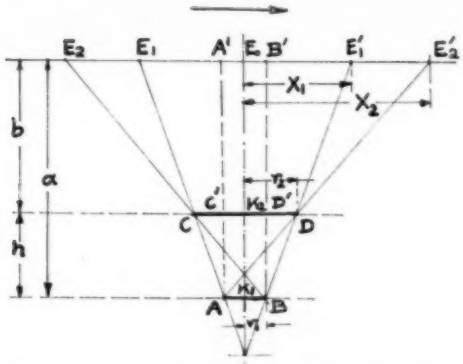

Diagramm 1. Projektionsverhältnisse des in der Schnittebene liegenden Objektes K_1, wenn zwischen ihm und dem Fokus ein zweiter strahlenabsorbierender Körper K_2 liegt.

strahlenabsorbierender Körper K_2 von ebenfalls kreisrunder Schnittfläche und dem Durchmesser $d_2 = 2\ r_2$ befinde sich zwischen K_1 und dem Röhrenfokus. Der Abstand zwischen K_1 und K_2 sei h, der zwischen K_1 und dem geradlinig bewegten Röhrenfokus a und der zwischen K_2 und dem Fokus sei b.

Legen wir durch die Endpunkte von K_1 und K_2 (A, B, C, D) Geraden, so schneiden diese die Fokusbahn in den Punkten E_1, E'_1 und E_2, E'_2. Wie aus Diagramm 1 ersichtlich, ergeben sich bei dem Versuch einer Schichtdarstellung von K_1 folgende drei Möglichkeiten:

1) Bewegt sich der Fokus zwischen den symmetrischen Punkten E_1 und E'_1 ($E_1E'_1 = 2\ x_1 = f_1$), so wird eine Schichtdarstellung von K_1 unmöglich, da hierbei der strahlenundurchlässige Körper K_2 eine Projektion von K_1 absolut nicht zulässt.

2) Bewegt sich der Fokus zwischen den symmetrischen Punkten E_2 und E'_2 ($E_2E'_2 = 2\ x_2 = f_2$), dann wird wiederum während des Fokusverlaufes von E_1 und E'_1 keine Projektion des schattengebenden Schnittes K_1 erfolgen. Während des Verlaufes zwischen E_2 und E_1, sowie zwischen E'_1 und E'_2 findet eine teilweise Projektion (*teilweise Schichtdarstellung*) statt, da nur in den Punkten E_2 und E'_2 eine totale Projektion von K_1 möglich ist.

3) Bewegt sich der Fokus auf der beliebigen Strecke über die Grenzpunkte E_2 und E'_2 hinaus, so erfolgt eine totale Projektion des K_1, selbstverständlich mit Ausnahme seines Verlaufes zwischen E_2 und E'_2, bei welchem, wie oben ausgeführt, nur eine teilweise oder keine Projektion von K_1 möglich ist.

Mathematische Beziehungen. Aus der Figur BE'_1B' folgt nach dem Strahlensatz:

$$\frac{D'D}{h} = \frac{B'E'_1}{a}; \qquad \frac{r_2 - r_1}{h} = \frac{x_1 - r_1}{a} \quad \text{da aber} \quad \begin{matrix} d_2 = 2\ r_2 \\ d_1 = 2\ r_1 \\ f_1 = 2\ x_1 \end{matrix}$$

folgt =

$$\frac{d_2 - d_1}{h} = \frac{f_1 - d_1}{a} \qquad \text{Gleichung 1 a)}$$

und

$$f_1 = \frac{a}{h}(d_2 - d_1) + d_1.$$

Die Gleichung 1 a) bestimmt den Grenzwert f_1 (d. h. die Strecke der Fokusbahn auf der die Schichtdarstellung von K_1 unmöglich ist) als Funktion der Grössen d_1, d_2, a und h.

Aus der Figur AE'_2A' folgt nach dem Strahlensatz:

$$\frac{C'D}{h} = \frac{A'E'_2}{a}; \qquad \frac{r_2 + r_1}{h} = \frac{x_2 + r_1}{a} \quad \text{da aber} \quad \begin{matrix} d_2 = 2\ r_2 \\ d_1 = 2\ r_1 \\ f_1 = 2\ x_1 \end{matrix}$$

folgt:
$$\frac{d_2 + d_1}{h} = \frac{f_2 + d_1}{a} \qquad \text{Gleichung 2 a)}$$

und
$$f_2 = \frac{a}{h}(d_2 + d_1) - d_1$$

Die Gleichung 2 a) bestimmt wiederum in Relation zu den Grössen d_1, d_2, a und h den Grenzwert f_2, d. h. die Strecke der Fokusbahn, auf der nur eine teilweise Projektion von K_1 möglich ist, nämlich einerseits zwischen E_2E_1 und andererseits zwischen $E'_1E'_2$.

Graphische Darstellung der Gleichungen 1 a) und 2 a) zur Bestimmung der Werte für f_1 und f_2 bei verschiedenen Grössen von d_1, d_2, a und h (Diagramm 2): In einem rechtwinkligen Koordinatensystem tragen wir die verschiedenen Grössen wie folgt an:

Auf der + x — Achse sei	h	(Masstab 1/1)
auf der + y — Achse sei	d_2	(Masstab 1/1)
	f	(Masstab 1/10)
bei Ermittlung von f_1 auch	d_1	(Masstab 1/1)
auf der — x — Achse sei	a	(Masstab 1/10)
auf der — y — Achse sei	d_1	(Masstab 1/1) bei Ermittlung von f_2.

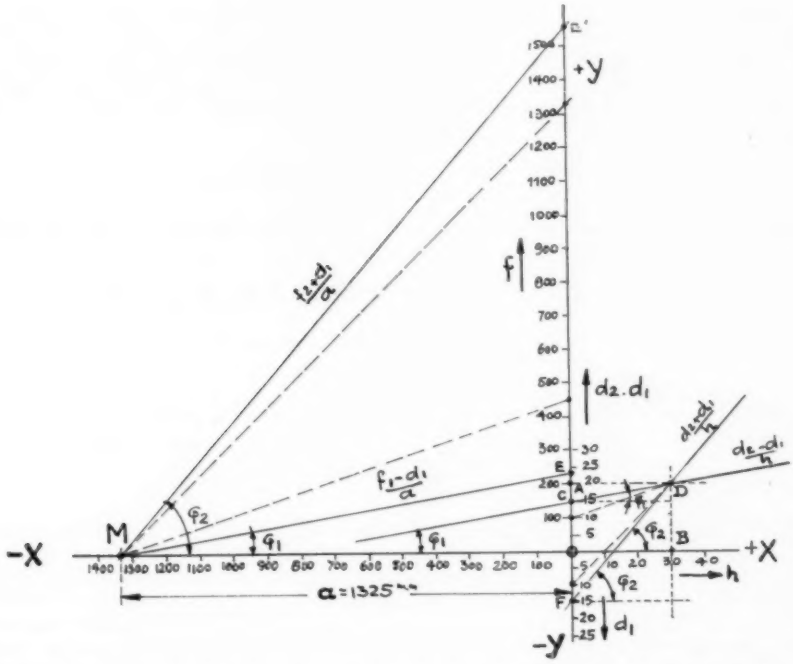

Diagramm 2. Graphische Darstellung der Gleichungen 1 a) und 1 b) zur Ermittlung der absoluten Werte für f_1 und f_2 bei verschiedenen Werten von d_1, d_2, a und h.

Bestimmung von f_1 (Schichtdarstellung unmöglich): Es sei $d_2 = OA$; $h = OB$ und auf der $+y$ — Achse sei $d_1 = OC$. Legen wir nunmehr zu den entsprechenden Koordinatenachsen Parallele durch die Punkte A und B, so liefert uns ihr Schnittpunkt den Punkt D. Verbinden wir die Punkte D und C, so können wir mit Hilfe des Neigungswinkels φ_1 dieser Verbindungsgeraden die linke Seite der Gleichung 1 a) bestimmen, weil $OA - OC = d_2 - d_1$. Es gilt somit:

$$\operatorname{tg} \varphi_1 = \frac{AC}{OB} = \frac{d_2 - d_1}{h}.$$

Durch den Punkt M (es sei $OM = a$) legen wir eine Parallele zu CD, welche die $+y$ — Achse im Punkte E schneidet. Die Neigung der Geraden ME ist charakterisiert durch das Verhältnis $\frac{OE}{OM}$. Da aber die Geraden CD und ME Parallele sind, haben sie den selben Neigungswinkel, d. h.

$$\operatorname{tg} \varphi_1 = \frac{OE}{OM} = \frac{d_2 - d_1}{h} = \frac{f_1 - d_1}{a} \text{ (nach Gleichung 1 a)}$$

da aber $OM = a$, folgt $f_1 - d_1 = OE$ und weiterhin

$$f_1 = OE + d_1$$

Bestimmung von f_2 (teilweise Schichtdarstellung): Es sei $d_2 = OA$; $h = OB$ und auf der $-y$ — Achse sei $d_1 = OF$. Legen wir nunmehr zu den entsprechenden Koordinatenachsen Parallele durch die Punkte A und B, so liefert uns ihr Schnittpunkt wiederum den Punkt D. Verbinden wir die Punkte D und F, so können wir mit Hilfe des Neigungswinkels φ_2 dieser Geraden die linke Seite der Gleichung 2 a) bestimmen, weil $OA + OF = AF = d_2 + d_1$. Es gilt somit:

$$\operatorname{tg} \varphi_2 \frac{AF}{OB} = \frac{OA + OF}{OB} = \frac{d_2 + d_1}{h}.$$

Durch den Punkt M legen wir eine Parallele zu FD, welche die $+y$ — Achse im Punkte E′ schneidet, sodass gilt:

$$\operatorname{tg} \varphi_2 = \frac{OE'}{OM} = \frac{d_2 + d_1}{h} = \frac{f_2 + d_1}{a} \text{ (nach Gleichung 2 a),}$$

da aber $OM = a$ gilt auch $f_2 + d_1 = OE'$ und somit

$$f_2 = OE' - d_1.$$

Arithmetische Beispiele (gestrichelte Linien in Diagramm 2): Es sei $d_2 = 20$ mm; $d_1 = 15$ mm; $h = 30$ mm und $a = 1{,}325$ mm. Aus dem Diagramm 2 ergibt sich:

$$OE = f_1 - d_1 = 235 \text{ mm und } f_1 = 250 \text{ mm}$$
$$OE' = f_2 + d_1 = 1{,}500 \text{ mm und } f_2 = 1{,}485 \text{ mm}$$

d. h. auf einer Strecke von 250 mm der Fokusbahn ist eine Schichtdarstellung des Querschnittes eines schattengebenden Körpers von 15 mm Durchmesser unmöglich, wenn sich zwischen ihm und dem Fokus im Abstand von 30 mm ein anderer schattengebender Körper befindet, dessen projizierte grösste Schnittfläche einen Durchmesser von 20 mm aufweist. Auf einer Strecke von 250 bis 1,485 mm der Fokusbahn erfolgt nur eine teilweise Schichtdarstellung, während bei einer Fokusbahn über 1,485 mm eine totale Darstellung gelingt.

Es sei $d_2 = 20$ mm; $d_1 = 10$ mm; $h = 30$ mm und $a = 1{,}325$ mm. Aus dem Diagramm 2 ergibt sich:

$$f_1 - d_1 = 440 \text{ mm und } f_1 = 450 \text{ mm}$$
$$f_2 + d_1 = 1{,}310 \text{ mm und } f_2 = 1{,}300 \text{ mm}$$

d. h. auf einer Strecke von 450 mm der Fokusbahn ist eine Schichtdarstellung des Querschnittes eines schattengebenden Körpers von 10 mm Durchmesser unmöglich, wenn sich zwischen ihm und dem Fokus im Abstand von 30 mm ein anderer schattengebender Körper befindet, dessen grösste projizierte Schnittfläche einen Durchmesser von 20 mm aufweist. Auf einer Strecke von 450 bis 1,300 mm der Fokusbahn erfolgt nur eine teilweise Schichtdarstellung, während bei einer Fokusbahn über 1,300 mm eine totale Darstellung gelingt.

Wenn $d_2 = d_1$, dann ist auch OA = OC. Ebenso wird AD = CD und verläuft parallel zur x-Achse. Die Gerade ME entspricht dann der x-Achse, sodass gilt

$$OE = O = f_1 - d_1$$
$$\text{und } f_1 = d_1.$$

Daraus ergibt sich, den Tatsachen entsprechend, dass dann zwischen zwei schattengebenden Objekten mit den gleichen grössten Durchmessern d_2 und d_1 (K_2 zwischen Fokus und K_1) die Schichtdarstellung von d_1 unabhängig vom Abstand h der beiden Körper, in jedem Falle unmöglich wird, wenn die Fokusbahn f_1 gleich oder kleiner als $d_2 = d_1$ ist.

Tafel 1

Beziehungen zwischen den Grössen h, d_1, d_2 und f_2 in den Fällen A und B

h	d_1	d_2 mm		f_2 mm	
mm	mm	Fall A	Fall B	Fall A	Fall B
10	5	12.0	12.0	2,215	2,235
	10	16.5	17.0	3,525	3,570
	15	21.5	22.0	4,845	4,895
15	5	15.0	15.0	1,770	1,790
	10	20.0	20.0	2,640	2,685
	15	25.0	25.0	3,520	3,575
20	5	18.5	18.5	1,550	1,570
	10	23.0	23.5	2,205	2,245
	15	28.0	29.0	2,860	2,920
25	5	22.0	22.0	1,420	1,435
	10	27.0	27.0	1,950	1,980
	15	31.5	32.0	2,460	2,520
30	5	25.0	25.5	1,325	1,350
	10	30.0	30.5	1,800	1,805
	15	35.0	36.0	2,190	2,260

d_1 = Durchmesser des darzustellenden Körpers K_1 in der Schnittebene.

d_2 = Durchmesser des verdeckenden Körpers K_2.

h = Abstand beider Körper (K_1 nach K_2).

f_2 = Fokusbahnlänge, auf der nur eine teilweise oder keine Projektion von K_1 möglich wird, wenn der Abstand Fokus-Schnittebene konstant 1,325 mm beträgt.

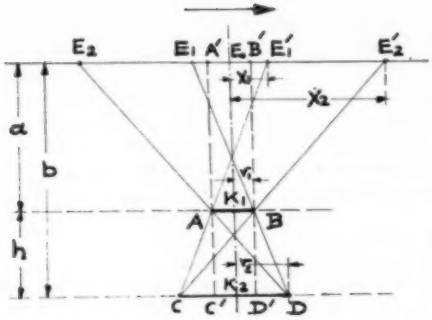

Diagramm 3. Projektionsverhältnisse des in der Schnittebene liegenden Objektes K_1, wenn es zwischen dem Fokus und einem zweiten strahlenabsorbierenden Körper K_2 sich befindet.

Fall B. In Diagramm 3 befindet sich der schattengebende, in der Schichtebene liegende Körper (K_1) mit dem grössten Durchmesser d_1 zwischen dem Fokus und dem zweiten schattengebenden Objekt (K_2) mit einem grössten Durchmesser d_2.

In diesem Fall lässt sich ebenso erkennen:

1) Die Strecke der Fokusbahn zwischen E_1 und E'_1 auf welcher eine Schichtdarstellung von K_1 unmöglich wird.

2) Die Strecke der Fokusbahn zwischen E_2 und E'_2 auf welcher eine teilweise Projektion von K_1 erfolgt.

3) Die Strecke der Fokusbahn über E_2 und E'_2 hinaus, auf der eine totale Projektion von K_1 möglich wird.

Mathematischen Beziehungen. Aus der Figur $CE'_1A'C'$ folgt nach dem Strahlensatz:

$$\frac{CC'}{h} = \frac{A'E'_1}{a}; \qquad \frac{r_2 - r_1}{h} = \frac{x_1 + r_1}{a} \qquad \text{da aber} \quad \begin{matrix} d_2 = 2\ r_2 \\ d_1 = 2\ r_1 \\ f_1 = 2\ x_1 \end{matrix}$$

folgt:

$$\frac{d_2 - d_1}{h} = \frac{f_1 + d_1}{a} \qquad \text{Gleichung 1 b)}$$

und

$$f_1 = \frac{a}{h}(d_2 - d_1) - d_1.$$

Aus der Figur $CE'_2B'D'$ folgt nach dem Strahlensatz:

$$\frac{CD'}{h} = \frac{B'E'_2}{a}; \qquad \frac{r_2 + r_1}{h} = \frac{x_2 - r_1}{a} \qquad \text{da aber} \quad \begin{matrix} d_2 = 2\ r_2 \\ d_1 = 2\ r_1 \\ f_2 = 2\ x_2 \end{matrix}$$

folgt:

$$\frac{d_2 + d_1}{h} = \frac{f_2 - d_1}{a} \qquad \text{Gleichung 2 b)}$$

und

$$f_2 = \frac{a}{h}(d_2 + d_1) + d_1.$$

Arithmetische Tafel zum Vergleich der beiden Fälle: Aus Tafel I können wir entnehmen, unter welchen Bedingungen eine Schichtdarstellung schattengebender Körper vom Durchmesser d_1 unmöglich, teilweise oder möglich wird wenn sie sich zwischen dem Fokus und einem zweiten schattengebenden Körper vom projizierten grössten Durchmesser d_2 befinden; die Fokusbahn $f = 900$ mm und der Abstand Fokus-Schichtebene $a = 1{,}325$.

Aus der Tafel lässt sich auch entnehmen, dass unter den oben genannten Bedingungen der Schichtphotographie eine Darstellung einer schattengebenden pathologischen Veränderung mit dem Durchmesser $d_1 = 5$ mm unmöglich ist, wenn sich zwischen ihr und dem Fokus im Abstand $h = 10$ mm eine zweite schattengebende Veränderung befindet, deren projizierter grösster Durchmesser $d_2 = 11.75$ mm (aufgerundet 12.0 mm) beträgt. Unter den gleichen Bedingungen erfährt diese pathologische Veränderung eine teilweise Schichtdarstellung dann, wenn die Länge der Fokusbahn zwischen 900 mm und 2,215 mm (f_2) beträgt. Eine totale Schichtdarstellung setzt voraus, dass die Fokusbahn grösser als 2,215 mm ist.

Vergleichende Untersuchung der Fälle A und B. Bei einem Vergleich der Fälle A und B finden wir eine nahezu völlige Übereinstimmung der Formeln 1 a) und 2 a) des Falles A mit den Formeln 1 b) und 2 b) des Falles B. Der einzige Unterschied besteht darin, dass wir im Falle B, $f_1 + d_1$ und $f_2 - d_1$ anstelle von $f_1 - d_1$ und $f_2 + d_1$ im Falle A finden. Deswegen sind graphische Darstellung und Lösung der Formeln 1 b) und 2 b) völlig die gleichen wie die der Formeln 1 a) und 2 a), nur wird im Falle B bei der Ermittlung von f_1 stehen $f_1 + d_1 = OE$ anstatt $f_1 - d_1 = OE$ im Falle A und bei der Ermittlung von $f_2 : f_2 - d_1 = OE'$ anstatt $f_2 + d_1 = OE'$. Deswegen gilt für die gleichen Werte von d_2, d_1, h und a folgendes:

$$(f_1)_A - d_1 = (f_1)_B + d_1 \text{ oder } (f_1)_B = (f_1)_A - 2\ d_1$$
$$(f_2)_A + d_1 = (f_2)_B - d_1 \text{ oder } (f_2)_B = (f_2)_A + 2\ d_1$$

(Wobei A und B die Indizes der jeweiligen Fälle darstellen.)

Somit lässt sich zusammenfassend sagen:

Eine Schichtdarstellung eines schattengebenden Körpers (K_1) mit dem Durchmesser d_1 ist unmöglich für eine Fokusbahn $(f_1)_A$, wenn sich zwischen ihm und dem Fokus ein zweites schattengebendes Objekt (K_2) mit dem Durchmesser d_2 im Abstand h befindet. Wenn sich der in der Schichtebene liegende Körper mit dem Durchmesser d_1 zwischen Fokus und dem zweiten strahlenundurchlässigen Objekt mit dem Durchmesser d_2 bei gleichem Abstande h befindet, wird die Schichtdarstellung für eine Fokusbahn $(f_1)_A - 2\ d_1 = (f_1)_B$ unmöglich.

Eine teilweise Schichtdarstellung eines Körpers K_1 mit dem Durchmesser d_1 ist möglich bei einer Fokusbahn $(f_2)_A$, wenn sich zwischen ihm und dem Fokus ein zweites Objekt K_2 mit dem Durchmesser d_2 befindet. Im umgekehrten Falle (K_1 zwischen K_2 und Fokus) findet eine teilweise Schichtdarstellung auf einer Strecke $(f_2)_A + 2\ d_1 = (f_2)_B$ der Fokusbahn statt.

Der geometrische Beweis ist aus Diagramm 4 zu entnehmen, wobei wiederum die Indizes A und B die Art des Falles bezeichnen.

Aus den Gleichungen 1 a), 2 a,) 1 b) und 2 b) folgt somit allgemein:

Für bestimmte Werte der Grös-

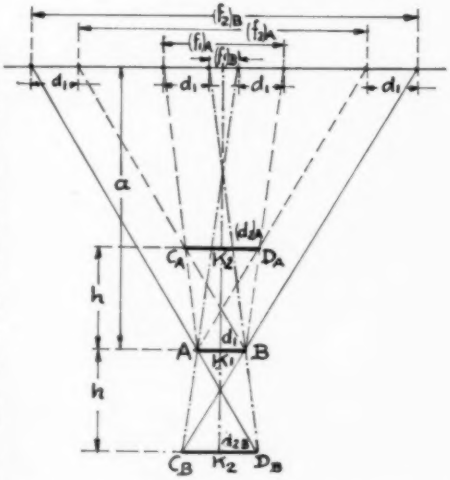

Diagramm 4. Vergleichende geometrische Untersuchung des Falles A und des Falles B.

sen d_1 und d_2 (Durchmesser der schattengebenden Objekte K_1 und K_2) wird bei gleichbleibendem Abstand h der Körper voneinander die Strecke der Fokusbahn, auf welcher nur eine teilweise oder keine Projektion von K_1 möglich ist, dem Abstand a (Fokus-Schnittebene) direkt proportional, d. h. sie wird umso kleiner, je kleiner a wird und umgekehrt.

Für bestimmte Werte der Grösse d_1 und d_2 (Durchmesser der schattengebenden Objekte K_1 und K_2) wird bei gleichbleibendem Abstand a (Fokus-Schnittebene) die Strecke der Fokusbahn, auf welcher nur eine teilweise oder keine Projektion von K_1 möglich ist, dem Abstand h (K_1 nach K_2) umgekehrt proportional, d. h. sie wird umso kleiner, je grösser h wird und umgekehrt.

Für bestimmte Werte der Abstände h (K_1 nach K_2) und a (Fokus-Schnittebene) wird die Strecke der Fokusbahn, auf welcher nur eine teilweise oder keine Projektion von K_1 möglich ist, nur von der Grösse der Differenz zwischen d_2 und d_1 bestimmt, d. h. sie wird umso kleiner je mehr sich der Durchmesser d_2 des verdeckenden Objektes dem des darzustellenden Körpers d_1 nähert und umgekehrt.

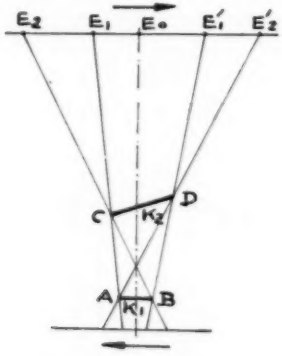

Diagramm 5.

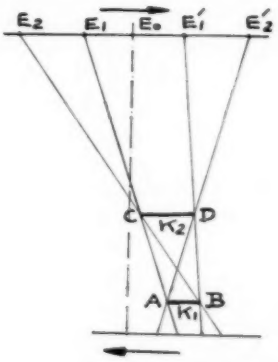

Diagramm 6.

Der Einfluss der Lage im Raum und der Neigung der beiden Körper K_1 und K_2 zueinander auf die Projektionsmöglichkeiten des in der Schnittebene liegenden Körpers K_1.

Fall C und D. Die Diagramme 5 und 6 zeigen, dass nicht nur die Grösse, sondern auch die Lage im Raum und die Neigung der beiden Körper zueinander, für die mögliche, teilweise oder unmögliche Schichtdarstellung eines dieser Körper bestimmend ist. Eine mathematische Untersuchung erübrigt sich nach den obigen Darstellungen.

Voraussetzungen für die Schichtdarstellung des Objektes K_1 in den Fällen A bis D

Anhand der obigen geometrischen Untersuchungen wurde die Frage der Freiprojektion von in der Schichtebene liegenden Objekten überprüft, wenn davor oder dahinter andere strahlenabsorbierende Körper liegen, deren Durchmesser grösser oder gleich dem des darzustellenden Körpers sind. Es konnte gezeigt werden, in welchen Fällen einer Schichtuntersuchung eine totale, teilweise oder keine Projektion eines in der Schnittebene liegenden schattengebenden Objektes unter den vorliegenden Bedingungen zu erwarten ist. Es fragt sich nunmehr, welche Möglichkeiten für eine Freiprojektion des in der Schnittebene liegenden Objektes dabei gegeben sind.

Abgesehen von der Anwendung harter Röntgenstrahlen, die in manchen Fällen zu einer Durchstrahlung des verdeckenden Objektes K_2 führen kann, bestehen für eine Freiprojektion des Objektes K_1 bei einer Schichtdarstellung folgende Möglichkeiten:

a) Die Ausnutzung der bei den Routineaufnahmen üblichen Schräg- bzw. Frontalprojektionen. Sie erweisen sich auch tatsächlich in vielen Fällen von Nutzen, wenn ihnen auch die bekannten Nachteile mannigfacher Störschatten anhaften.

b) 1. Die Vornahme von Schichtaufnahmen mit ausreichender Fokusbahn (die also über die Grenzpunkte E hinausgeht).

2. Die Verkürzung des Abstandes Fokus-Schnittebene (Abstand a).

Beide Möglichkeiten haben jedoch, abgesehen von rein technischen Schwierigkeiten, den Nachteil, dass sie eine Verzerrung und Unschärfe der abzubildenden Objekte zur Folge haben.

3. Die Schichtdarstellung ein und derselben Schnittebene bei verschiedenen Richtungen der Fokusbahn, d. h. etwa bei einer sagittalen Schichtbilduntersuchung der Lunge, dass die Fokusbahn bei gleichbleibender Schichttiefe parallel zur Schnittebene mehrere Winkel zur Längsachse des Thorax durchläuft. Wenn wir nämlich uns vor Augen halten, dass in der Praxis die Objekte K_1 und K_2 pathologischen Veränderungen entsprechen, die je einen grössten und kleinsten Durchmesser aufweisen, liegen für das darzustellende Objekt die günstigsten Verhältnisse dann vor, wenn die Fokusbahn parallel zum kleinsten Durchmesser des verdeckenden Körpers verläuft. Da wir jedoch nicht imstande sind, vor der Schichtuntersuchung eine entsprechend exakte Lage und Grössenbestimmung mehrerer Veränderungen in einem Organ, z. B. der Lunge, vorzunehmen, erscheint uns die Anwendung dieser Methode, nicht nur in Bezug auf die Vermeidung von Verwischungsschatten ([1], [2], [3]) sondern auch aus reinen Projektionsgründen als die günstigste Schichtbildmethode.

ZUSAMMENFASSUNG

Anhand geometrischer Untersuchungen wurde die Frage der Freiprojektion von in der Schichtebene liegenden Objekten überprüft. Es konnte gezeigt werden, in welchen Fällen einer Schichtuntersuchung eine totale, teilweise oder keine Projektion zu erwarten ist. Für die Praxis ergab sich hinsichtlich der Projektionsmöglichkeiten die Forderung einer Schichtuntersuchung derselben Ebene unter verschiedenen Fokusbahnrichtungen.

SUMMARY

The problem of the free projection of an object in a tomographic layer was studied by geometric methods. It was found possible to predict whether total or partial projection or non-projection of the object was likely to occur. In practice this demands that the examination be carried out in the same plane with different movements of the tube.

RÉSUMÉ

L'auteur reprend l'étude géométrique du problème du dégagement des objets situés dans le plan de coupe. Il démontre dans quelles conditions tomographiques on doit s'attendre à une image totale, partielle ou nulle. Il en résulte en pratique que, pour tenir compte des possibilités de dégagement, il est nécessaire de tomographier le même plan avec différentes directions de balayage.

LITERATUR

Burger, G. C. E. und van Weel, I. G. A.: Die Möglichkeit zur planigraphischen Darstellung der intrathorakalen Lymphdrüsen. Fschr. Röntgenstr. 57 (1938), 143.

Gaubatz, E.: Beiträge zum Schichtaufnahmeverfahren (Stratigraphie). Fschr. Röntgenstr. 58 (1938), 447.

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BOOK REVIEWS

On Parallax and Variations in the Stereoscopic Image With a View to Stereofluoroscopy. By Tauno Mannila. 107 pp., 40 figs., 12 tables. Acta radiol. Suppl. 139 (1956). Sw. Kr. 25.—.

After a short survey of the general conditions for stereoscopic vision followed by a discussion of the problems encountered in stereoradiography and stereofluoroscopy, parallax is dealt with in detail both from theoretic and practical viewpoints.

In the chapter dealing with stereo-effect, the author suggests that the parallax of a stereoscopic system be expressed in the form of the ratio l/h, in which l = the stereobasis and h = the distance of the stereobasis from the object, both in centimetres. In this way it is easy to compare the stereo-effects of different systems without having to measure the angles in degrees. For practical purposes, the author provides a formula from which the desired stereo-effect can be produced. As regards the use of Marie-Ribaut's formula in radiologic stereoscopy, the author concludes that when this formula is applied a thin object at a long distance gives an unnaturally great and a thicker object at a short distance an unnaturally small stereo-effect.

The next chapter deals with the effect of parallactic difference on the position of the stereo-image. While the stereo-effect depends on the projection parallax, the position of the stereo-image with regard to the projection surface is determined, in its turn, by the viewing parallax. The mutual position of the stereo-image components in the projection surface, is of great importance in this respect. The stereo-image may be seen either in front or at the back of the projection surface, or wholly or partially at the projection surface.

The effect of parallactic difference on the fusion of stereo-image components in viewing is discussed. If this difference becomes very great the difference between the distances of accommodation and convergence may grow so much that fusion fails. Taking into account that when parallactic differences grow, the distance of the stereo-image position from the screen also increases, there is a twofold reason for avoiding a large parallactic difference.

The second main section of the work deals with the variations which may occur in connection with stereofluoroscopy. In addition the section describes the possible variations when stereo-roentgenograms are viewed with stereobinoculars. The author has also taken stereoscopic roentgenograms with no perspective, and roentgenograms in which the rays converged to a point outside a movable roentgen tube. In this connection, the concept of an angle of projection is introduced. The perspective is determined according to the type (positive or negative) and size of the projection angle. The investigation showed that perspective in the stereo-image variations may be correct but the sagittal view inverted or vice versa.

Autoreview.

A Radiologic Study of the Brain Circulation by Rapid Serial Angiography of the Carotid Artery. By Torgny Greitz. 123 pp., 28 figs. Acta radiol. Suppl. 140 (1956). Sw. Kr. 30: —.

The purpose of this study is to analyze the possibility and the value of determining the circulation time through the brain by means of rapid serial angiography. By evaluating the sources of error when this method is used to record time processes, a correct basis for this investigation is obtained. Statements have been made in the literature, that angiography is unsuitable for studies of the circulation time. It has, inter alia, been suggested that the volume of the contrast medium increases the pressure in the carotid artery and in this way the angiographic procedure might conceivably influence the cerebral circulation. Moreover, it has been suggested that the injection influences both the local circulation in the injected vessels, either by provoking spasm or dilatation, and the systemic circulation.

It has therefore been considered important to examine the influence of the angiographic procedure on the circulation. This has been accomplished by recording the ECG and the intra-arterial pressure, the latter in the carotid as well as in the femoral artery during the puncture and the injection of contrast medium. These investigations have shown that the systemic circulation is not unaffected by the angiographic procedure. Rapid serial angiography has therefore to be compared with another method of measuring the circulation time. A technique has been developed whereby circulation times are determined with small amounts of isotopes. This method, which is described in detail, has no influence on the systemic circulation. If the results obtained by rapid serial angiography and by isotope studies are compared, it is found that a significant correlation exists between them.

In order to evaluate the value of rapid serial angiography in intra-cranial lesions, the normal sequence of contrast filling has to be determined. This sequence is found to be so regular and orderly that there is justification to use it as a basis for the evaluation of circulatory conditions in pathologic cases.

By using the author's method, it is possible to determine not only the circulation time through the brain but also through a diseased region. The relation between the circulation time through the brain and through the lesion gives in arterial occlusions an idea of the degree of retardation of the flow; in arterial venous malformations an indication of the degree of shunting; and in tumours certain information about their pathologic nature. The conclusion is reached that rapid serial angiography is of value in practical neuro-radiologic work.

Autoreview.

Technique de Radiodiagnostic. Par R. Ledoux-Lebard et J. Gracia-Calderon. 1,150 pages, 764 ill. Masson et Cie., Paris 1956.

This large book is the second edition of a work first published in 1943. During the 10-year interval, the progress in roentgen diagnostics has been enormous, necessitating enlargement and a thorough revision of the subject matter.

The authors' aim has been to present a complete survey of methods used in the field of medical radiology. It should thus be possible for the radiologist, confronted with a particular problem of examination, rapidly to survey all the methods available. For those who seek additional information and knowledge, a restricted bibliography, with no claims to completeness, is appended. As the book is primarily directed to a French-speaking public, the references in the main comprise publications in the Latin languages.

The book consists of two main parts, a general and a special. In the former, the fundamental principles of roentgen techniques, the classical standard method, and the different complementary specific methods are surveyed. The origin and properties of roentgen rays are first briefly discussed together with factors influencing the production and quality of the image. This is followed by a presentation of such special investigation methods as teleradiography, stereoradiography, and tomography. The scanographic method is even mentioned. Then follows a survey of different contrast media, of equipment in dark rooms and of the kind of work carried out there. Finally, an analysis is made of protection measures that are necessary in radiologic work.

In the special part, the authors describe in detail positioning and the different projections that may be applied, and instructive drawings illustrate the procedures. The joints, spine, and skull are first treated, and thereafter investigations of the brain, spinal cord, heart, and blood vessels. To perform such complicated examinations, however, it must be stressed that more detailed descriptions of techniques are needed than those incorporated in this textbook, although the survey is quite extensive. This need has also been anticipated by the authors, and adequate references are given. The treatment of techniques used in the examination of the digestive and respiratory tracts, and of the urogenital organs, is however, most detailed.

The book ends with an index in alphabetical order consisting of subjects and of authors covered in the references.

The comprehensiveness of the work is admirable and bears witness of the authors' extensive knowledge of the literature. The whole field of roentgen diagnostic techniques with its enormous number of divisions is covered. Methods and results are recorded in an objective manner and the authors have refrained from giving their personal grading of the values of the separate methods. The readers are left to make their own choice of method in the collections described.

It should be of extreme value in roentgen departments with a broad field of activity to have access to this textbook as 'un instrument de travail'.

Folke Knutsson.

La Tomographie Axiale Transversale. Par G. Bonte, M. Brenot et G. Trinez. 165 pages, 135 figures. Doin et Cie, Paris 1955. 2,200 frs.

The first part of the book, after an introductory historical survey, deals with the principles and techniques of the tomographic method, with particular regard to centering. The authors express the view that secondary grids are unnecessary; an incident angle of 25° is recommended.

The next section contains detailed analyses of such matters as layer thickness, sharpness, and image distortion. The analysis of the factors leading to image distortion of the object is, in the reviewer's opinion, particularly valuable. Clear and instructive illustrations show how the different objects mutually affect each other; the sources and significance of parasitic images are discussed in detail. That it is important for the interpretation of tomograms to know the basic facts concerning the sources of distortion and the origin of superadded images seems evident.

In a third part, the clinical applications of the method in examinations of the thorax, abdomen, and skeletal parts are dealt with; main importance is placed on the first. Applications in radiotherapy are also mentioned. The fourth part which concludes the book contains an extensive case material with illustrations.

The theoretical portions of the work are richly illustrated, the tomograms also being profuse and excellent. The authors emphasize that it is especially in the field of

thoracic examinations that the method is indicated and that it should be regarded as a complementary procedure. Its limitations in its present stage of development are pointed out.

The book can be recommended to all who wish to gain knowledge of the theoretical aspects of the method and their significance in clinical applications.

Herman Lodin.

RÖNTGENDIAGNOSTIK DES HÜFTGELENKS. Von R. Glauner und W. Marquardt. 168 S., 195 Abb. Georg Thieme, Stuttgart 1956. DM 57.—.

The roentgenology of the hip-joint is described in more detail than in the large textbooks of roentgen diagnostics. In comparison with the latter, the presentation is more compact and comprehensive and the book therefore serves a purpose. Furthermore, the text matter is short and the references are few, the main emphasis being placed on the illustrative material which is good. Fractures are dealt with only as contributory factors in causing arthrosis.

The book has more the character of a roentgenographic atlas than a monograph; it has no pretensions to completeness. In the reviewer's opinion, however, the chapter dealing with roentgen techniques and anatomy is too brief. The primary objectives in roentgen diagnostics are, of course, to obtain images which may lead to a clear conception of anatomic detail and to avoid confusing distortion of the projections or superposition of irrelevant skeletal parts. If the right views have been produced, the diagnosis is often clear. This applies no less to the hip-joint in children and young people. The expression "Lagerung nach Lauenstein" cannot be regarded as adequately defining the positioning for a lateral view, and the authors make no differentiation between a lateral view of the epiphysis or one of the collum. An illustration of this may be obtained from a comparison of Fig. 72 b, a lateral view of the epiphysis, with Fig. 74 b, which is more a view of the collum and in which it is hard to judge the state of the epiphysis. (Cf. Acta radiol. Suppl. 110, 1954.)

The directions for measuring the CE-angle (WIBERG) are not sufficient to enable the reader to perform such a measurement, and the reference is not correct.

The book is beautifully printed.

Lars Billing.